Interim Session, American College of Chest Physicians
Denver, Colorado, November 30, December 1, 1952

VOLUME XXII NUMBER 5

DISEASES

of the

CHEST

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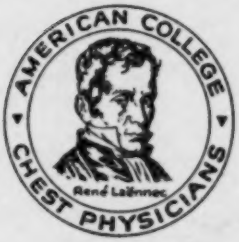

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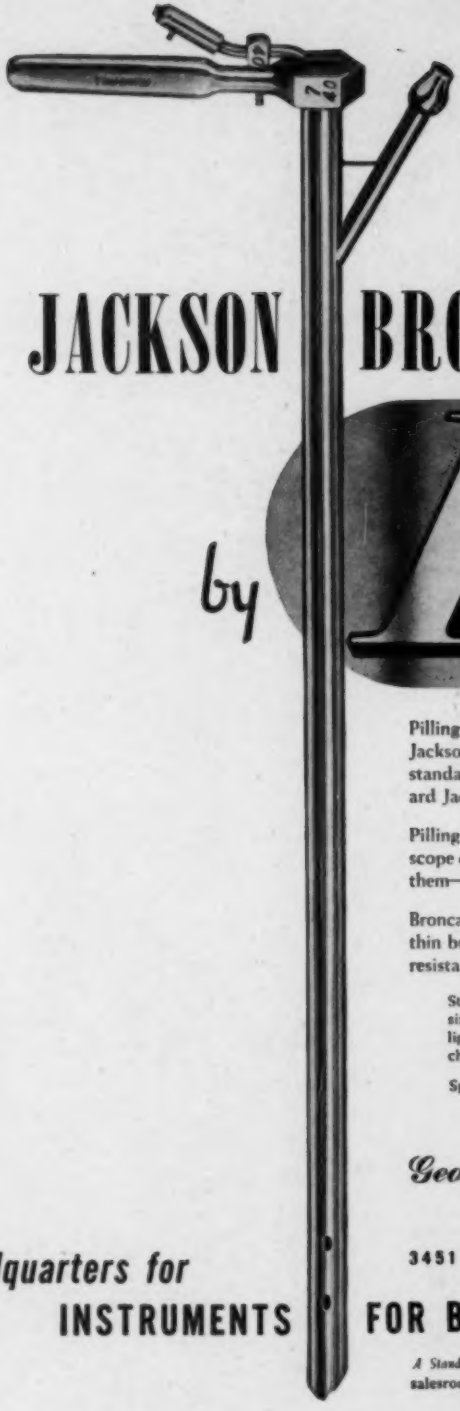

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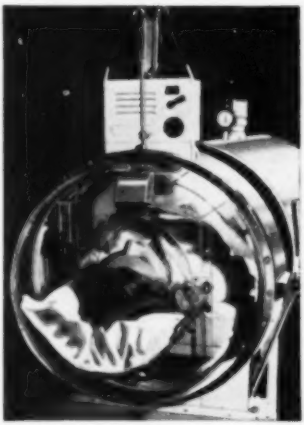

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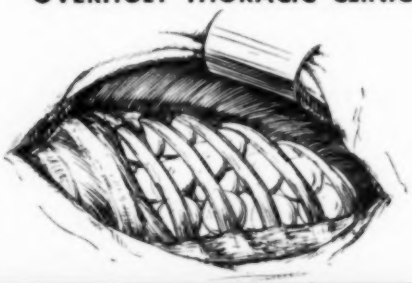

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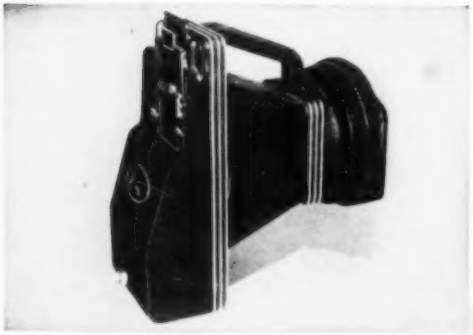

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(For more information about 'Neo-Penil', see page 26)

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Response: The amount of expectorate decreased but slightly.

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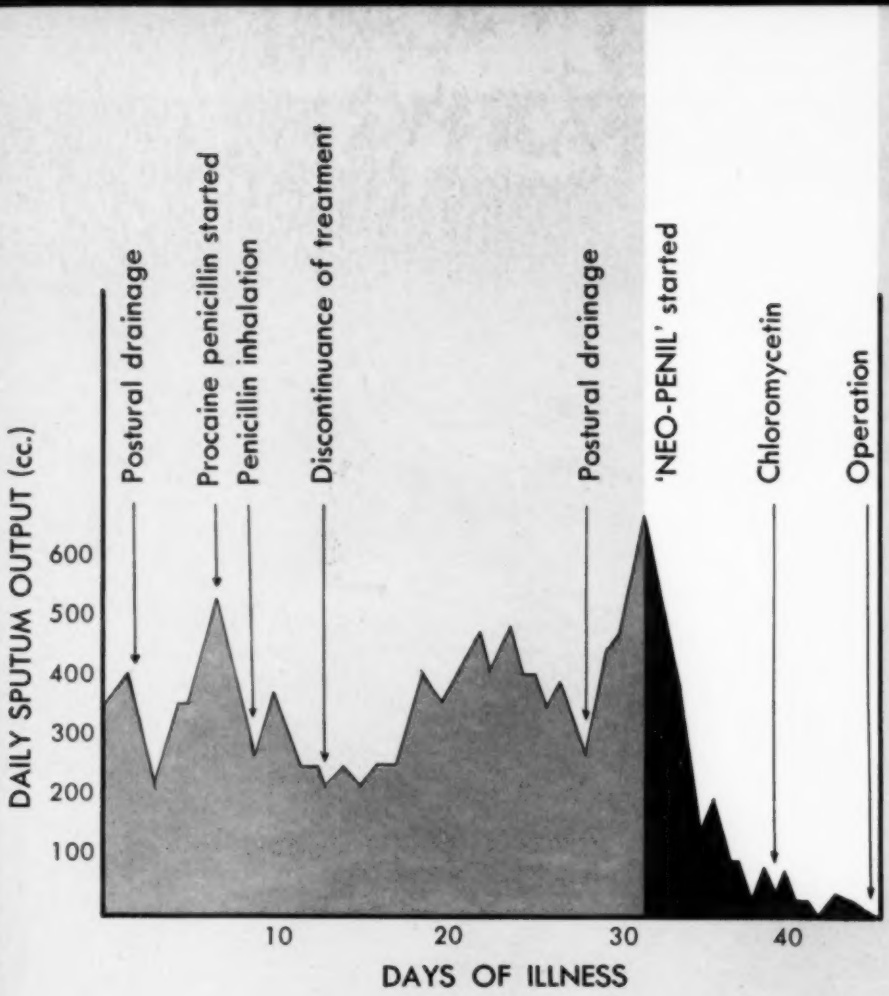
Response: After 6 days, sputum volume was reduced from 600 cc. to 50 cc. per day. At this time sputum culture revealed penicillin-resistant bacteria and chloromycetin was given, 0.5 Gm. every 6 hours for 5 days. The sputum volume was further reduced, and it was felt safe to operate.



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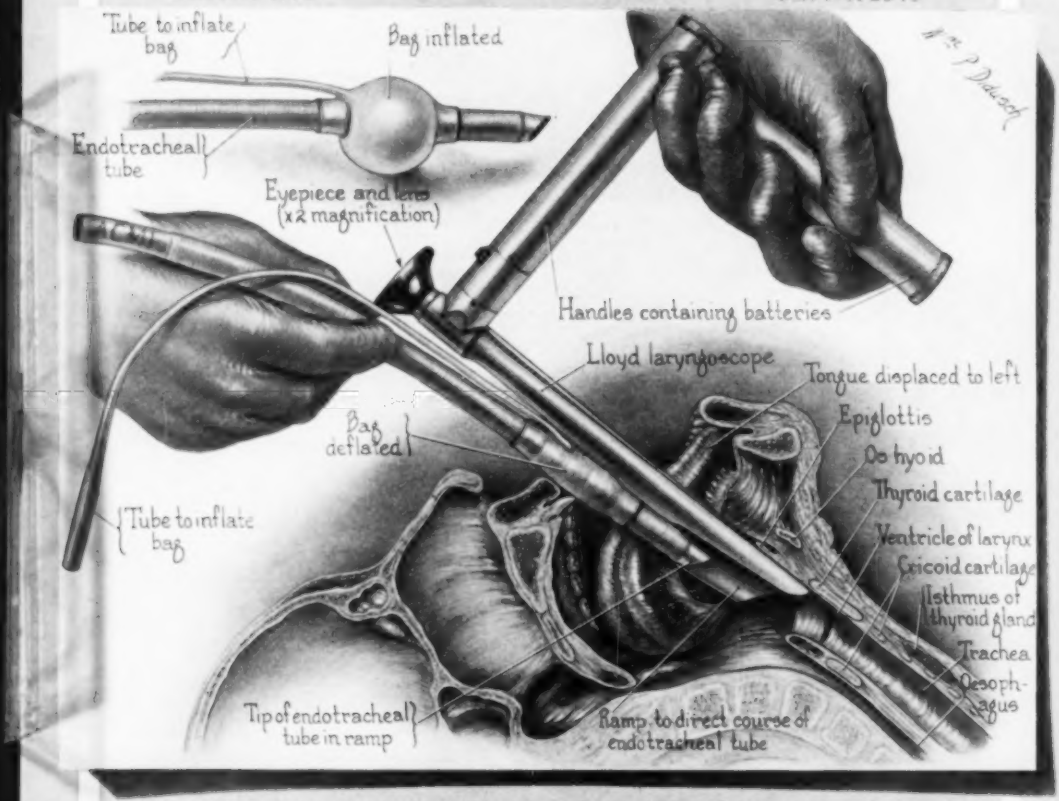

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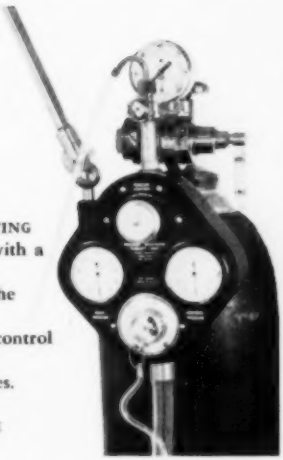

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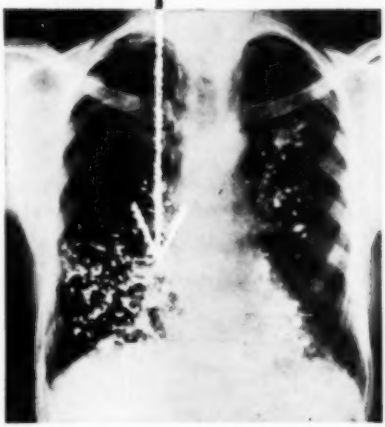
"... the diagnosis can only be fully confirmed by x-ray of the chest after the instillation of iodized oil (lipiodol) into the air passages."[3]



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1. Yater, W. M.: Fundamentals of Internal Medicine, ed. 3, New York, Appleton-Century-Crofts, 1949, p. 315.
2. Myers, J. A., and McKinlay, C. A.: The Chest and the Heart, Springfield, Ill., Charles C Thomas, 1948, p. 307.
3. White, B. V., and Geschickter, C. F.: Diagnosis in Daily Practice, Philadelphia, J. B. Lippincott Co., 1947, p. 419.

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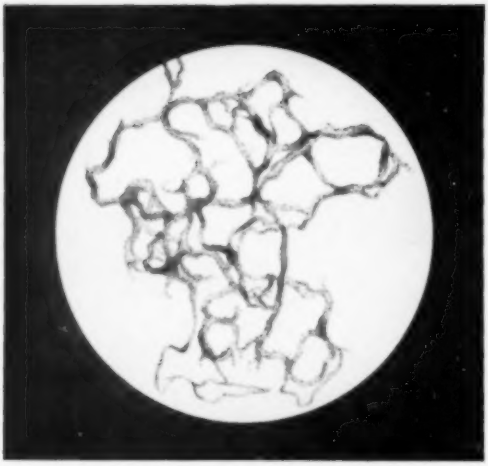

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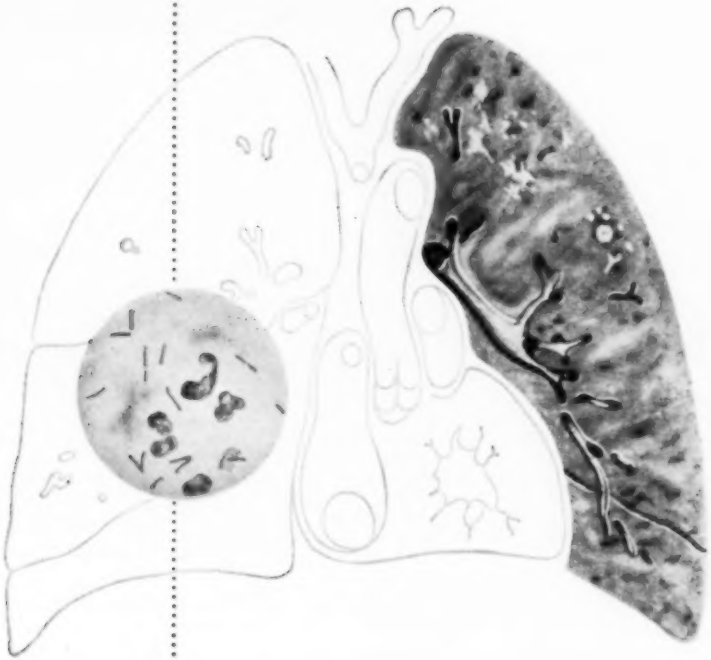

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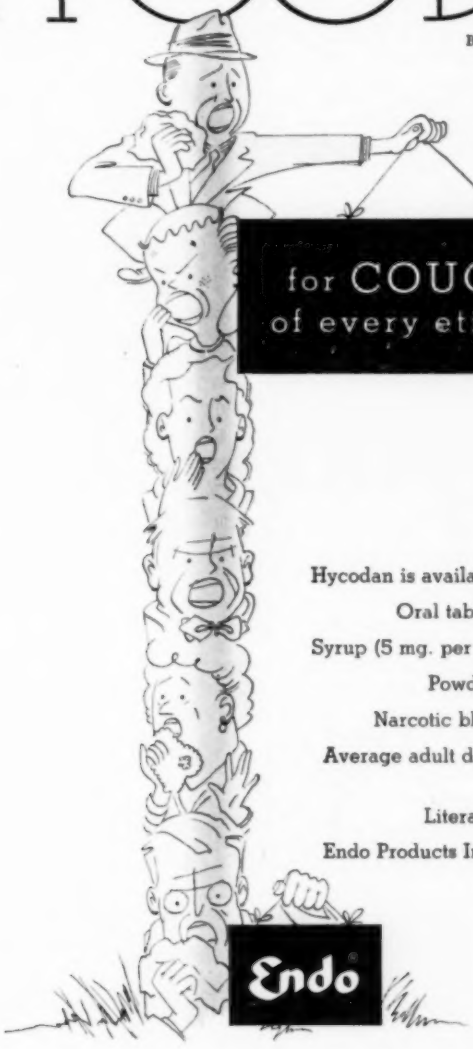

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DISEASES *of the* CHEST

VOLUME XXII NOVEMBER 1952 NUMBER 5

An Evaluation of Extrapleural Pneumonolysis*

Based on a Follow-up Study of Seventy Cases with Lucite Plombage

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Introduction

Thoracoplasty is accepted today as the best surgical collapse procedure in the treatment of tuberculosis; it has reached this position by a steady rise in popularity in the last half century. Its limitations have been defined and are generally respected. But because of the traumatic nature of this procedure, the fact that it causes such obvious deformity and reduces function of otherwise good pulmonary tissue, an attempt has repeatedly been made to find a procedure which could replace thoracoplasty in suitable cases. Extra-pleural pneumonolysis has been called upon again and again to fill this gap; but it has not been accepted generally even for a very limited field of application, nor is there any concensus regarding its value in the treatment of tuberculosis. From time to time, series have been presented, some with very good results, as recently by Brantigan and Rigdon;[1] others with less satisfactory results have been reported, the most recent by Cutler.[2] The difference in results is quite obviously due to their respective selection of cases. Occasionally, additional factors are introduced into the discussion mainly with regard to the type of plombage material used. Unfortunately this has confused the issue even more.

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It would hardly be worthwhile, in our opinion, to present a follow-up study on a series published earlier merely to show that the late results of this operation are still satisfactory. This has been shown before by Arnold[3] and Roberts[4] and would at this time merely increase the confusion. It is rather in an attempt to elucidate some of the important aspects of extra-pleural pneumonolysis on the basis of our knowledge of the procedure and in the light of our experience with it that we present this evaluation.

It would seem to us that the anatomical features of the operation and the pathological factors involved are so potent with regard to the results and complications of the procedure that the type of plombage material, provided it is inert enough, will not influence the results in one way or another to any marked degree. Although we are presenting a series in which Lucite balls have been used for plombage, we believe that our conclusions apply to extra-pleural pneumonolysis in general, whether the space is filled with air or any other inert plombage material.

The fundamental strength of thoracoplasty lies in the fact that it achieves the conditions which the body aims to arrive at when attempting to arrest tuberculosis. It permits collapse of the diseased area, enabling the fibrotic process to contract the destroyed parenchyma, while at the same time it leaves the rich blood supply of the chest wall in contact with the lung. Maurer and Chenebault[5] described in detail the mechanism by which the vessels of the chest wall can act as a supplementary circulation for the periphery of the lung.

The inherent weakness of extra-pleural pneumonolysis derives from the fact that this anatomical consideration is being ignored and the periphery of the lung is separated from the rich blood supply potential of the chest wall. The fact that the lung is left covered by two layers of pleura does not in any way improve the situation, as all these structures, lung and pleurae, depend after extra-pleural stripping on the hilar blood supply for their existence. If this supply should fail at any time due to the pathological process, the mere thickness of avascular tissue will not prevent its necrosis and perforation of a pulmonary cavity into the space. Some surgeons, as Alarcon[6] for example, strip in cases with dense adhesions as far externally as possible to include the deep layer of the costal periosteum and leave the lung covered with a thick layer of soft tissue severed from its blood supply. On the basis of the anatomical and pathological considerations, it is difficult to see how this would make the procedure any safer.

With a clear understanding of this weakness of extra-pleural pneumonolysis, we are presenting a number of conclusions on the value of this procedure based on a three year (on the average)

follow-up study of 70 cases with Lucite plombage. These conclusions are not based on the empirical results of success and failure alone, but on the anatomical and pathological features of the procedure in combination with experience gained from this series and its results.

Presentation of Series

In 1946, extra-pleural pneumonolysis with Lucite ball plombage began to be used as a permanent collapse procedure at the National Jewish Hospital in cases otherwise suitable for thoracoplasty. It was hoped that the procedure would in time replace thoracoplasty in suitable cases and thus reduce deformity and loss of function. From 1946 until 1948, extra-pleural pneumonolysis was performed in 70 patients; four additional cases received Lucite balls as a prosthesis after resection. As the results in the early cases of this series were very encouraging, the indications were widened and many cases were included merely because they were unsuitable for thoracoplasty or any other procedure. In April 1948, Grow and Dwork[7] reported their early experiences with this technique. At the annual meeting of the National Tuberculosis Association in 1949, the early results of the whole series were presented by Grow, Hurst and Perlmutter.[8] A careful follow-up study of these cases has been made so that today we have complete information of the late results on 67 of the 70 cases. Of the other three cases, one man (H.I.) has a satisfactory x-ray film finding, but information on sputum is not available.

As can be seen from Table I, the 70 cases divide into three main groups: Group 1: Unilateral plombage performed as a definitive procedure; Group 2: Bilateral plombage; Group 3: Preliminary plombage with resection under the Lucite plomb to follow later as a planned procedure.

Group 1, which includes 54 cases, divides again into 49 patients in whom only plombage had been performed, and five for whom additional resection was done because of failure of the collapse to convert the patient's sputum. Of the 49 patients on whom the plombage was done as the only procedure, 27 had moderately advanced disease (in 21 of whom only one lung showed evidence of disease), while there were 22 patients with far advanced disease (in 21 of whom both lungs showed evidence of the disease). Thirty of the 49 cases would be considered suitable for thoracoplasty, while seven cases in this group carried contra-lateral pneumothorax (all of whom had far advanced disease). In five cases the pulmonary function was borderline.

All but three cases of the whole series had positive sputum pre-operatively. In the great majority of the cases there was

TABLE I: EXTRA-PLEURAL PNEUMONOLYSIS
With Lucite Plombage (70 Cases)

Group	1 UNILATERAL PLOMBAGE INTENDED AS DEFINITIVE a Plombage Only	b Additional Resec.	Total	2 Plan. Plom. and Resec.	3 Bilateral Plombage	Total
Number of Cases	49/54 = 91%	5/54	54/70	7	9	70 = 100%
Moderately Advanced Disease	*27/49 = 55%	2/5	29/54	2/7	0	31/70 = 45%
Far Advanced Disease	**22/49 = 45%	3/5	25/54	5/7	9/9	39/70 = 55%
Suitable for Thoracoplasty	30/49 = 60%	5/5	35/54	4/7	0	39/70 = 55%
Contralateral Pneumothorax	7/49 = 15%	0	7/54	1	0	8/70
Borderline Pulmonary Function	5/49	—	5/54	—	—	—

*21 unilateral plus 6 bilateral, distribution of disease.
** 1 unilateral plus 21 bilateral, distribution of disease.

definite evidence of cavitation, most of them less than three centimeters in diameter. In 16 cases there was cavitation, three to nine centimeters in diameter. More details of the case material, the operative technique (anterior approach), and the post-operative course can be found in the earlier report.[8]

Results

With the cooperation of many physicians and clinics throughout the country, we have been able to stay in contact with 67 of the 70 cases. We have received x-ray film and sputum reports at intervals, as well as reports on their activity. In the majority of cases, we have seen recent x-ray films ourselves. The present follow-up is on the average just over three years since operation; the earliest operation having been done over five years ago while the latest one was performed two years and three months ago. Table II shows the results of the three groups at present. Of the 54 patients with unilateral plombage approximately 72 per cent have negative sputum and can now be considered inactive. For a series which includes so many complicated cases, these results must be considered very satisfactory. This is true even though there are, at this time, 10 deaths in the total series, six of whom are in the group of unilateral plombage. A detailed discussion on these deaths will show that apart from those who died from complications of additional resection, most of them were extremely poor risks for whom nothing else could have been done and who were only included because of the widening of the indications.

Before discussing the complications and failures in greater detail, it would seem worthwhile to divide the result of the 54 unilateral plombage cases according to the extent of their disease. The first subgroup (Table III) consists of 29 cases with moderately advanced disease; all (except one case, G.M., with severe congenital scoliosis) would be considered suitable for thoracoplasty. In two of this group, resection had to be done because of failure of the collapse to convert the patient's sputum. Subgroup 2 includes 25 cases of far advanced disease (Table IV), all but two of whom would be considered unsuitable for thoracoplasty, seven of these were carrying contra-lateral pneumothorax and five had borderline pulmonary function. In three cases, it was necessary to do additional resection under the plomb. The results in both of these groups are presented in two divisions: The early results on the average one year after operation, and the late results now about two years later. It will be seen that in both series only a small number have changed their position with regard to the results (see Tables III and IV).

The division of these 54 cases into two subgroups, as outlined,

TABLE II: RESULTS (70 Cases)

Group	I a Unilateral Plom. Only 49	I b Resec for Plom. fail. 5	Total 54	II Bilateral Planned 9	III Plom. and Res. Planned 7	Total 70
Inactive	**32	5	39=72%	5	3	45=67%
Arreseted Occ. pos. cult.	2	—		—	—	2
Active Impr.	*3	—	3	—	*†3	6
Reactivated	1	—	1	—	—	1=6%
Broncho-pleural Fistula	2	—	2	***1	—	3
Dead	*6=12%	—	6=11%	1	††3	10=14%
No Follow-up	3	—	3	—	—	3

*Including one case with contralateral pneumothorax.

**Including five cases with contralateral pneumothorax.

***Resection.

†For various reasons resections not performed as planned.

††Two cases with resections.

The results are expressed in the terminology found in "Diagnostic Standards and Classification of Tuberculosis," 1950, edited by the National Tuberculosis Association.

is particularly instructive because it divides them into very good and very poor risk cases. In the 29 good risk cases, approximately 90 per cent became negative and arrested their disease as a result of the operation. In one case (S.M.), the sputum was not converted, while two cases are excluded due to lack of follow-up. The results now, two years later, are still very good. About 80 per cent are still inactive. One patient (L.S.) recently had a positive culture, and has, therefore, been taken out of the group of inactives. One case (L.B.) has reactivated her disease on the contra-lateral side, which failure we must accept considering that we are dealing with as serious and recrudescent a disease as tuberculosis. Two patients in this group developed late broncho-extra-pleural fistulae, one three and the other three and a half years after surgery. We believe that these two cases are of very great importance, and we will expand our discussion on them later. There were no other complications of importance, nor have there been any deaths to date in this subgroup.

In the 25 with far advanced disease who were generally poor or very poor risk cases, the results are still surprisingly good. Sixty per cent arrested their disease as the result of the operation; three

TABLE III (Subgroup 1)

MODERATELY ADVANCED DISEASE (29 Cases)

Unilateral Plombage as Definitive Procedure

All but one case (severe congenital scoliosis) suitable for thoracoplasty.			
Two cases had additional resection.			
Twenty-three cases, unilateral distribution of disease.			
RESULTS			
	Early Results	Late Results	
Inactive	*26 = 90%	*22	= 80%
Arrested	—	1	
Active, Improved	1	1	
Reactivated	—	1	= 10%
Broncho-pleural Fistula	—	2	
No Follow-up	**2	**2	
Dead	—	—	

Fourteen per cent of Cases Shifted Their Position

*Including two cases with additional resection.

**One case x-ray report satisfactory. No information on sputum.

Note: There is a shift of four cases which earlier were considered inactive to arrested (1), reactivated (1), and bronchopleural fistula (2).

did not convert their sputa, but two of them were improved to the extent that now, two years later, they have a consistently negative sputum on smear, one of them (B.Y.) with an occasional positive culture while the other (M.O.) has had no recent culture made. Apart from the deaths, which we will discuss later, there were two failures at the time of the early results, one (O.M.) whose sputum stayed positive and who was considered unimproved, and the other (J.C.) with a broncho-pleural fistula due to a large cavity breaking into the extra-pleural space within a few weeks after the operation. In the late results of this subgroup, there is actually a larger number of arrested and converted patients, 68 per cent, while the two failures (the unimproved and the broncho-pleural fistula) have since died, both more than two years after surgery, the first (O.M.) possibly not from his tuberculosis. If we

TABLE IV (Subgroup 2)

FAR ADVANCED DISEASE (25 Cases)

Unilateral Plombage as Definitive Procedure

All but two cases unsuitable for thoracoplasty.			
Seven cases carrying contralateral pneumothorax.			
Five cases of borderline pulmonary function.			
Three cases had additional resection.			
Twenty-three cases, bilateral distribution of disease.			
Eight cases, cavitation 3 to 9 centimeters.			
	RESULTS		
	Early Results	Late Results	
Inactive	*†15=60%	*†15	=68%
Arrested	—	2	
Active, Improved	**3	**1	
Active, Unimproved	1	—	= 8%
Broncho-pleural Fistula	1	—	
No Follow-up	1	1	
Dead	**4	**6	=24%

Fifteen per cent of Cases Shifted Their Position

*Including three resections.

**One case with contralateral pneumothorax.

†Including five cases with contralateral pneumothorax.

Note: The shift from early to late results is as follows: two of the "active improved" group moved to the "arrested" category, while both the case in the "active unimproved" and in the "bronchopleural fistula" group subsequently died.

consider that of this very poor risk group 68 per cent are today inactive or arrested, we cannot but feel that the results are very satisfactory.

Of Group 2 (Table II), nine cases of bilateral plombage, three cases had additional resection. Of the other six, synthetic sponge[9] has been used as plombage material for the second side in three cases, while one case had a successful unilateral oleothorax at the time of her admission. Of these nine cases, five are inactive, while one has a persistent broncho-pleural fistulous tract following a right upper lobectomy under the plomb. Of the three patients who died, two underwent resection and developed broncho-pleural fistulae, while one died at the time of removal of Lucite spheres and thoracoplasty done for a spontaneous broncho-extra-pleural fistula. This case (K.S.) will be discussed in detail in the section on deaths. We consider the five cases of success, in the small group of nine, highly satisfactory as no other procedure would have been possible for these bilateral cases. Since that time we have performed bilateral extra-pleural pneumonolysis with synthetic sponge on six patients, all of whom are negative, one woman (E.W.) after a left upper lobectomy under the plomb.

Of the seven cases of Group 3 (Table II), plombage and planned resection, three did not undergo resection; of these, one (J.M.) refused while the other two were so much improved but otherwise such poor risks that it was decided to be satisfied with partial success. All three still have positive sputum. Three cases are inactive, while one (C.F.) died as the result of a broncho-pleural fistula after the resection. In this case too, it would have been better judgement to have been satisfied with the partial success of the plombage. His condition did not permit resection before collapse was performed.

Resection in Combination with Lucite Spheres (Table V)

Twelve resections (four pneumonectomies and eight lobectomies) were done under lucite plombage to which are added four cases (three pneumonectomies and on lobectomy) in whom lucite spheres were introduced as a prosthesis at the time of resection. In the unilateral and bilateral plombage groups, eight resections were done because of failure of the extra-pleural pneumonolysis to control the disease and convert the sputum. Of the seven patients on whom excisional surgery was planned from the beginning, only four had resection performed. One patient (J.M.) refused resection while the other two had been improved by the plombage alone and were otherwise such poor risks that it was preferred not to perform the resection as had been intended at the beginning. All these three patients have a positive sputum, but are otherwise

improved. In two cases in whom pneumonectomy was performed under the Lucite plomb, additional spheres were inserted into the intra-pleural space after the resection; both patients are well. Of the four cases of resection in whom lucite spheres were used as a prosthesis, one had carcinoma in combination with tuberculosis, both diagnosed before operation. This patient (H.S.) developed a broncho-pleural fistula, had the lucite spheres removed, and died later of empyema.

Of the total of 16 patients who underwent resection, 11 arrested their disease and are inactive, four are dead (all of them had a broncho-pleural fistula at the time of death), while one patient (L.G.) with resection of a lobe after bilateral plombage is alive with a persistent broncho-pleural fistulous tract. In an additional three cases who underwent resection in combination with synthetic sponge, either as a prosthesis or under an earlier sponge plombage, there is another case (K.W.) in whom a broncho-pleural fistula developed, which necessitated removal of the sponge and thoracoplasty. He has a persistent fistula and empyema.

Although all these cases were streptomycin resistant and therefore more liable to develop broncho-pleural fistula after resection, as has been shown recently again by Murphy,[10] the incidence of this serious complication in practically a third of the cases must be considered unusually high. We cannot but place some of the responsibility for the high proportion of broncho-pleural fistulae on the extra-pleural pack. In our opinion, we are not justified to add the risk of infection which is introduced with the foreign body to the already considerable risks of resection per se. It is true that several patients were lucky enough to get by without broncho-pleural fistula after resection under lucite spheres and

TABLE V: RESECTIONS
In Combination With Lucite Balls

	Unilateral Plombage	Bilateral Plombage	Planned Resections	Resec. with Prosthesis	Total
	54	9	7	4	74
Resection Done	5	3	4	4	16
Inactive	5	—	3	3	11
Reactivated	—	—	—	—	—
Alive With Broncho-pleural Fistula	—	1	—	—	1
Dead	—	2	1	1*	4**

*Tuberculosis and carcinoma of bronchus.
**All deaths had a broncho-pleural fistula at time of death.

managed to avoid the deformity of thoracoplasty. In any case of plombage in whom we would consider the need for excisional surgery, we should, in the future, however, prefer to remove the foreign body and perform thoracoplasty before attempting the resection.

Complications

For this purpose we have divided the total series (see Table VI), into slightly different groups: Group 1 in which only unilateral plombage was done includes three cases of the group in whom resection was planned, but was not performed for one reason or another; Group 2 in which bilateral plombage was done; and Group 3 which includes all the resections under the lucite plomb. Apart from early or late broncho-extra-pleural fistulae with empyema, complications were few and unimportant. Fluid formation in the immediate post-operative period and some rise in temperature in that period which were discussed in the earlier report[5] must be considered part of the post-operative course and not complications of the operation. Non-specific infection of the extra-

TABLE VI: COMPLICATIONS

	Unilateral Plombage 52*	Bilateral Plombage 6	Resections 12	Total 70
Contralateral Spread	1 (cleared)	—	—	1
Infection in Space	1 (cleared)	—	—	1
BPF early	2 (dead)	1 (dead)	4 (3 dead)	7
BPF late	2 (alive)	—	—	2
TOTAL DEATHS	**6	1	3	10

*Forty-nine unilateral plombage plus three of planned group in which no resection was done.

**Including deaths not due directly to the operation.

TABLE VII: RESULTS AND COMPLICATIONS OF CASES WITH CAVITATION, 3 CENTIMETERS AND MORE (15 Cases)

	Plombage 11	Additional Resection 4	Total 15
Arrested and Well	*4	2	6
Unimproved, Sputum Positive	4 (1 dead)	—	3
Broncho-pleural Fistula	3 (3 dead)	2 (2 dead)	—
Deaths	4	2	6

*In three cases 3 centimeter cavitation, one case 4 centimeter cavitation.

pleural space has only occurred in one case (F.M.) and cleared after intensive local antibiotic therapy. One other case (L.M.) had a contra-lateral spread post-operatively which cleared and the patient can now be considered inactive. Broncho-pleural fistula in combination with empyema, on the other hand, has taken a severe toll of the group. Of the seven early fistulae, three were due to spontaneous break through of a large cavity into the extra-pleural space, and all three are dead.

The risk of complications and failure is definitely increased in cases with large cavitation. The results in 16 cases in whom there were cavities of three to nine centimeters in diameter show this very clearly (Table VII). One patient (J.B.) amongst those with large cavitation died post-operatively. At autopsy he was found to have a bilocular heart and may therefore be excluded in this connection. Only four patients of the group of 15 converted their sputum as the result of the extra-pleural plombage and are well today. Of the remaining 11 patients, four underwent additional resection, two of whom became negative, while two died as the result of the resection. Three of the remaining seven patients developed spontaneous early broncho-extra-pleural fistula (within six months of the operation) and are dead. In the whole series, these three were the only patients with this serious complication. One patient (M.O.) died two years after the operation with persistently positive sputum. Of these 15 with large cavitation, therefore, six patients are inactive, three are alive with positive sputum, while six are dead. It is obvious even from these small figures that although the prognosis of the disease is so much worse when large cavitation is present, extra-pleural pneumonolysis does not hold out much promise in these cases.

Returning to the complications of the total series (Table VI), we find that in addition to the three patients with early spontaneous broncho-extra-pleural fistula who died, two who had been considered inactive developed this complication at a much later date, one (A.D.) three and the other (F.M.) three and a half years after operation. Both these cases had tomography done before operation and showed no evidence of either large or peripheral cavitation nor were any dense adhesions encountered at the time of stripping. One (A.D.) has had the lucite spheres removed recently and is awaiting resection. In the other case (F.M.) a broncho-extra-pleural fistula was diagnosed recently by the presence of air in the extra-pleural space. This is recognized by the fact that the lucite spheres stand out more clearly, the air acting as a contrast medium.[11] This sign can be visualized clearly by comparing Figures 2 and 3.

Of the 12 patients who underwent resection in combination

with lucite spheres either as an earlier plombage or as a prosthesis at the time of resection, four developed a broncho-pleural fistula. Of these, only one is alive, a patient (L.G.) who had right upper lobectomy after bilateral plombage.

Deaths

Ten patients in the series are dead, only one (J.B.—bilocular heart) died in the immediate post-operative period (five days after operation); the others died six months to two and a half years after surgery. While no attempt is being made to reduce the significance of the 10 deaths, it is desirable to determine to what extent these deaths were avoidable and how much the procedure can be blamed for these failures. Three deaths which are most directly related to the operation itself (K.E., S.K., and J.C.) were due to spontaneous break through of the cavity into the extra-pleural space in the early period. All three had large cavities with no normal lung parenchyma peripheral to the lesion.

Case 1: J.C., is a 25 year old, white female, with a history of one year's symptoms. On admission, she had bilateral symmetrical upper lobe infiltration with multiple cavities of about nine centimeters in aggregate diameter on each side (Figure 1). Pneumothorax was attempted but was unsuccessful and the cavities increased in size while the patient showed signs of intermittent toxicity. Bilateral extra-pleural pneumonolysis with lucite plombage was planned in an attempt to halt the progression of the disease. On October 10, 1948, the extra-pleural pneumonolysis with lucite plombage was done on the right (Figure 2). Her generally poor condition following the operation precluded performance of the same operation on the left side. About three months after operation, she developed a broncho-extra-pleural fistula under the lucite plomb. She continued to run a persistent fever throughout her stay in the hospital. She developed signs of inflammation of the uterine adnexae, probably tuberculous in origin. In October 1949, she was taken home by her husband in a generally poor condition. The lucite spheres were removed and thoracoplasty was done about a year later in another sanatorium where she died in March of 1951.

Comment: This case demonstrated a typical situation in which we would consider today extra-pleural pneumonolysis, in any form, absolutely contraindicated, as would probably the great majority of surgeons.

Case 2: O.E., a 38 year old male, had only a few months history of symptoms referrable to the chest. X-ray film on admission revealed bilateral extensive disease with a giant cavity of about nine centimeters in the left upper lobe (Figure 4). The cavity appeared to become smaller on bed rest. Six months after admission, he had several hemoptyses, a post-hemoptoic spread to both bases, and received streptomycin with successful clearing. After unsuccessful pneumothorax and in view of the residual left upper lobe cavity which had in effect not become smaller to any marked degree (Figure 5), extra-pleural pneumonolysis with lucite

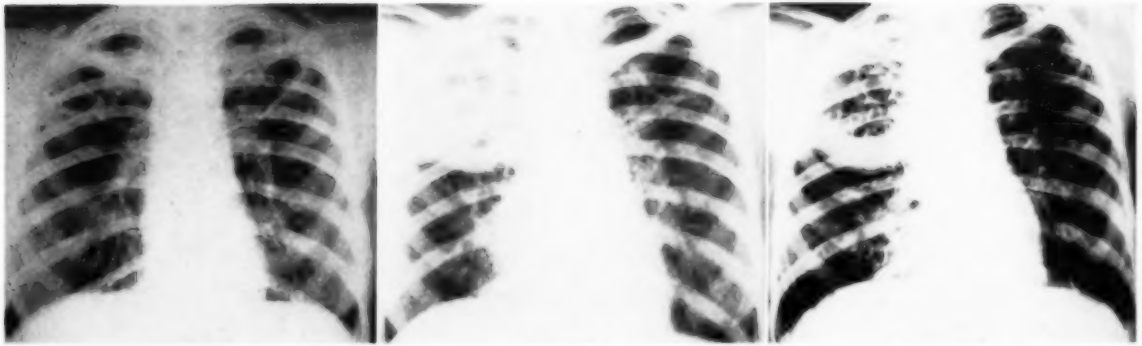

FIGURE 1 FIGURE 2 FIGURE 3

Figure 1, Case 1: (J.C.), pre-operative x-ray film, bilateral multiple large cavities.—*Figure 2, Case 1:* (J.C.), after right extra-pleural pneumonolysis with lucite plombage. Note the persistent large cavity under the extra-pleural shelf as well as the cavities under that for which no operation could be done because of her poor condition.—*Figure 3, Case 1:* (J.C.), six months after operation, broncho-extra-pleural fistula has developed with fluid and air in the space. Air is recognized by the clear outline of the lucite balls as compared with Figure 2.

plombage was done on the left on May 11, 1948. After an uneventful recovery, the sputum became negative. He was discharged at his insistence in September 1948. Three months later, he was re-admitted because of a broncho-extra-pleural fistula which had developed in the meantime. The lucite spheres were removed and a five rib thoracoplasty was performed with the fistula being clearly visable at the time of operation. The patient did not recover from the operation, and at post-mortem examination pulmonary embolism with bilateral broncho-pneumonia was found.

Comment: This is another case with giant cavitation. Though the cavity had decreased in size pre-operatively to some extent, the blood supply of the lung tissue between the cavity and the pleura had obviously not improved to any marked degree.

Case 3: S.K., a 51 year old white male, was admitted with bilateral far advanced tuberculosis, with a history of six years. Bilateral pneumothoraces had been tried but were unsuccessful. There were bilateral cavities of three centimeters in diameter (Figure 6). Extra-pleural pneumonolysis with lucite plombage was planned. The right side was done on March 3, 1948, followed by the left four weeks later. About four months after surgery, a lucite ball extruded through a sinus from the extra-pleural space on the right side. An attempt was made to repair the defect with tantalum wire mesh but was unsuccessful. The lucite spheres were removed and a five rib thoracoplasty performed, but the patient died post-operatively from anoxia. He had developed an extra-pleural empyema with broncho-extra-pleural fistula, by perforation of the cavity on the right into the space.

FIGURE 4 FIGURE 5

Figure 4, Case 2: (O.E.), X-ray film on admission, giant cavitation on left side.—*Figure 5, Case 2:* (O.E.), cavity though smaller still of considerable size. No lung tissue visable between the peripheral aspect of the cavity and the pleura.

Comment: Although the size of the cavities in this case were not excessive (three centimeters in diameter), the tomogram (Figure 6) shows that there was no normal lung parenchyma between the cavity and the pleura on the right. This would mean that the peripheral aspect of the cavity wall has a poor blood supply and is prone to become necrotic after extra-pleural stripping causing a broncho-extra-pleural fistula.

These three cases of early spontaneous broncho-extra-pleural fistula would have been avoided if we had selected our cases to exclude those with large cavitation and peripheral disease, as we would do today. They died after additional surgical intervention, such as removal of lucite balls and thoracoplasty, but these procedures were done as a result of the broncho- pleural fistula and empyema. These deaths must therefore be blamed on the extra-pleural pneumonolysis.

Three other cases (C.F., K.N., and L.W.) developed broncho-pleural fistulae after resection under the lucite plomb. Before the resection was done, the patients were in good condition with no complications regarding the space, even though the extra-pleural pneumonolysis had not converted their sputum. While they were failures from the point of view of the plombage, they cannot be blamed as death on this procedure. On the other hand, it would seem to us that resection under lucite plomb is more dangerous

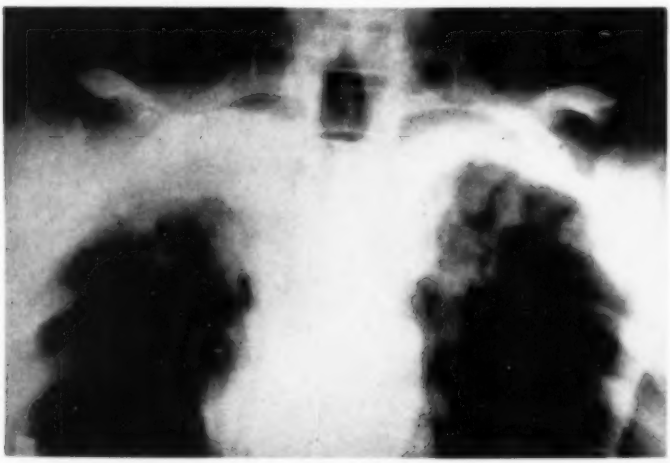

FIGURE 6. *Case 3:* (S.K.), tomogram 9 cm. from the back showing bilateral cavitation. The tissue between the cavity on the right and the periphery is obviously not healthy areated lung. This cavity perforated later into the space.

than resection in general, and therefore, in our opinion, not justifiable.

Of the four deaths remaining, one (J.B.) died five days after operation suddenly and was found to have a bilocular heart at autopsy. This was a boy of 17 years in a completely hopeless state of health, and though it was realized that he had congenital heart disease, the diagnosis of bilocular heart was not made pre-operatively. This case is being reported separately.[12]

The second case (D.A.) carried a contra-lateral pneumothorax. His sputum turned negative soon after extra-pleural pneumonolysis, but broke down some time later with progression of the disease and died from massive hemorrhage. His was a case completely unsuitable for any other procedure and was selected on that basis.

The third case (J.S.) was one with very poor function with right heart strain for whom nothing else could have been done. He became more dyspneic after the operation and died six months later in heart failure.

The fourth case (O.M.) died about two and a half years after surgery. The operation had not converted his sputum. He was a severe diabetic, and the only information available regarding his death is that he was admitted to a mental hospital, where he died soon after his admission, presumably in diabetic coma. He, too, would not have been suitable for any other surgical procedure, and because of the extensive changes in the contra-lateral lung, resection could not be considered seriously after the failure of the extra-pleural pneumonolysis.

With the only death in the immediate post-operative period in this series due to a bilocular heart (J.B.), the operative mortality of extra-pleural pneumonolysis must be considered low. This coincides with the experience of many surgeons. The main complication leading to death at a later date is, in our experience, the development of broncho-extra-pleural fistula due to peripheral involvement of the lung. This risk can be reduced considerably by a careful selection of cases.

Fate of Lucite Balls and of the Space

Lucite balls have been removed up to date in 11 cases and in one case (F.M.), a late broncho-pleural fistula, we recommended their removal but the patient left against advice.

In two cases, the lucite spheres were removed and thoracoplasty done as a procedure of choice after resection. In the nine other cases, the removal was done for broncho-pleural fistula, which was in four cases the result of spontaneous break through to the extra-pleural space (three early, dead; one late, alive). In

five cases a broncho-pleural fistula developed after additional resection; only one of them is alive today.

Discussion

In attempting to evaluate extra-pleural pneumonolysis as a collapse procedure in the treatment of tuberculosis of the lung, we believe that the figures we have presented above permit a number of important deductions. First of all, it has been shown that this procedure can control the disease and convert the sputum in a high proportion of cases. Similar figures have been presented before and most surgeons with experience with this operation will agree on this point. The fact that the early results are better than those after three years is equally true with any surgical procedure or other form of treatment in tuberculosis. The results have been achieved with a minimal amount of trauma and deformity and the amount of functional lung tissue lost is very small. This latter point has been shown quite clearly by Dressler, Bronfin and Grow[13] in our pulmonary function laboratory.

The advantages of extra-pleural pneumonolysis are well known and have been described in detail.[8] The only serious disadvantage of the operation derives from the fact that by stripping the parietal pleura away from the chest wall, the most diseased part of the lung is deprived of its natural emergency mechanism and left to the mercy of the pathological process.

There are three phases in relation to extra-pleural pneumonolysis during which this weakness may lead to the perforation of a cavity into the space with the formation of a broncho-extra-pleural fistula. This complication can occur as an accident during the operation when stripping is difficult and there is a cavity on the peripheral aspect of the lung. This accident has not happened in our series. As we, like many other surgeons, believe that such cases are unsuitable and no attempt should be made to continue the stripping under such conditions, this complication, it would seem to us, is avoidable.

The second period of danger is within the few months following the operation when the peripheral aspect of the lung, largely devitalized at the time of operation, becomes necrotic and the cavity perforates into the extra-pleural space. In our series, there have been three such cases, all of whom developed fistulae within six months of the operation; two died soon after the complication occurred, while the third died only recently, about two and one half years after surgery. In all three cases, there was large or giant cavitation without any normal parenchyma between the cavity and the pleura.

On the basis of the theoretical consideration described above

with regard to the anatomical and pathological factors and the confirming experience from these three cases, we believe that this type of case is absolutely contraindicated for this procedure. This opinion is shared today by the majority of surgeons who perform this operation. We cannot accept the opinion as expressed by Cutler[2] that such a broncho-extra-pleural fistula and empyema may not be too severe a price to pay for collapsing a lung in a poor risk case. In our experience, this complication has always been a very serious one. Fortunately it is possible to weed out these cases, either before or, at the latest, during the operation.

A careful x-ray work-up including tomography will indicate the condition of the peripheral aspect of the lung in the majority of cases and permit pre-operative selection. Any unsuitable case which for some reason is not recognized on x-ray inspection can be picked up at the time of operation by the presence of dense adhesions in the extra-pleural plane. Such adhesions indicate the need of the periphery of the lung for the blood supply of the chest wall.[5] Under such conditions, it is preferable not to attempt to strip the pleura from the chest wall forcibly but to discontinue the operation immediately. Many experienced surgeons have stressed this point earlier,[14,15] while others have demonstrated the increase of serious complications when stripping is persisted with in these cases.[16] If these points are strictly adhered to, we believe that the risk of broncho-extra-pleural fistula in the immediate post-operative period is small.

It is true that by limiting our indication to this extent we exclude a considerable number of patients who could get a satisfactory collapse from this procedure in all probability without developing broncho-extra-pleural fistula. These patients, if unsuitable for thoracoplasty, would need this operation more than any one else. However we do not believe that any surgical procedure can be called upon to fill the gap left by other procedures. Any re-inclusion of these cases must discredit the operation in the eyes of the internist and surgeon alike. If in any specific case it is felt that the risk involved is justifiable in an otherwise hopeless situation, such a case has to be judged on its own merits and not included in a series for evaluation.

On the basis of our knowledge of the anatomical and pathological factors involved, it is obvious that these factors continue to act even after the two early danger periods have passed and that the possibility of the development of a late broncho-extra-pleural fistula is always present. In the 29 cases of moderately-advanced disease, practically all suitable for thoracoplasty and excellent risks, two patients who had converted their sputa as a result of the operation and were considered inactive have developed bron-

cho-extra-pleural fistulae three years or more after the operation. Since both had small cavities not peripherally placed as proved by tomography and no marked adhesions were encountered at the time of their operation, they must be considered well-selected cases. Recently an additional case from the private practice of one of the authors (J.B.G.) has undergone pleural pneumonectomy for broncho-pleural fistula which developed two and a half years after extra-pleural pneumonolysis.

This late complication cannot, in our opinion, be blamed on the lucite spheres. A change which occurs three years or more after the operation cannot be due to the inert packing material but must be blamed on the factor with the potentiality of change, in this case, the disease process within the lung.

When we consider the ever-present possibility of local reactivation of the disease, it is obvious that if such exacerbation under the shelf should choose to extend in the direction of the extra-pleural space, there would be nothing to prevent it from perforating into it. The same exacerbation occurring under a thoracoplasty would of course come up against the healthy and vascularized thoracoplasty plate which would help the lung tissue to limit the disease and would not permit perforation of a peripheral cavity. Unfortunately there is no way of deciding preoperatively which case might choose to re-activate under the extra-pleural shelf after years of satisfactory collapse. With such theoretical knowledge confirmed in our series by two cases, such a possibility must be considered an ever-existing danger in all cases in whom there is diseased lung under the extra-pleural shelf.

Based on this argument, it would seem appropriate that no patient whose disease is suitable for collapse by thoracoplasty should be considered for extra-pleural pneumonolysis. This procedure is only indicated therefore in cases in whom primary thoracoplasty is either absolutely or relatively contraindicated because of poor physical condition, limitation of function, deformity, and the need for bilateral surgical collapse. In these cases, after careful selection to exclude large or peripheral cavitation, the procedure should be planned, ideally in every case, as a temporary collapse only. After stabilization of the shelf, limited thoracoplasty, just enough to obliterate the space, should be performed. This will re-establish contact between the periphery of the lung and the chest wall with its rich blood supply potential. In this respect, we are in full accord with Hoyt and Tate[16] who made the same recommendation. It is obvious that with the limitations set above, the operation is indicated only in a comparatively small number of cases. Should further experience, however, confirm that the deformity and loss of pulmonary function of the thoraco-

plasty following the temporary collapse of extra-pleural pneumonolysis is considerably reduced, the operation may be indicated for quite a number of patients for whom otherwise classical thoracoplasty would need be done.

In patients in whom no thoracoplasty, either primary or following extra-pleural pneumonolysis, could be considered because of their very poor condition, the inherent risk of the procedure as a permanent collapse will have to be weighed against the poor prognosis of the unchecked disease. Since the incidence of late broncho-extra-pleural fistula in our series, as well as in others, has not been very high nor the complication so serious at that time, we believe that under such conditions this may be considered a justifiable calculated risk. In cases with giant and peripheral cavitation, the high proportion of poor results combined with the considerable risk of an early and, in our experience, more serious type of broncho-extra-pleural fistula makes, in our opinion, the risk prohibitive. In these cases when thoracoplasty is contraindicated for other reasons, the only active treatment at present short of resection is cavernostomy.

SUMMARY

1) Extra-pleural pneumonolysis can control tuberculous disease in the lung in a high proportion of cases.

2) Its main weakness is due to the anatomical and pathological factors involved.

3) For the purpose of avoiding the complications of an early broncho-extra-pleural fistula, a thorough x-ray work-up including tomography should be done to exclude giant or peripheral cavitation.

4) If during the extra-pleural stripping, dense adhesions are encountered, the operation should be discontinued and no attempt be made to separate them forcibly.

5) To avoid the risk of late broncho-extra-pleural fistula, the operation should be planned ideally in every case as a temporary collapse procedure and thoracoplasty, sufficient to collapse the space, be performed as soon as the extra-pleural shelf has stabilized satisfactorily (about six months).

6) The extra-pleural plomb increases the danger of bronchopleural fistula after resection under it, and it is recommended that the plomb be removed and thoracoplasty be done before proceeding with resection. Cases who have successful resection under the extra-pleural plomb will not necessarily require removal of the plomb and thoracoplasty.

RESUMEN

1) La neumolisis extrapleural puede controlar tuberculosis del pulmón en una proporción elevada de casos.

2) Su principal punto débil se debe a los factores anatómicos y patológicos participantes.

3) Con el propósito de evitar una fístula broncoextrapleural temprana debiera ser hecha una revisión completa mediante rayos-x incluyendo tomografía, para excluir la caverna gigante o periférica.

4) Si durante la operación extrapleural, se encuentran adherencias densas, la operación deberá ser interrumpida y no deberá de tratarse de separarlas por fuerza.

5) Para evitar el peligro de la fístula broncoextrapleural tardía la operación debiera ser planeada idealmente en cada caso como un colapso temporal y una toracoplastía, suficiente para efectuar el colapso del espacio, sería efectuada tan pronto como la coraza extrapleural se haya estabilizado satisfactoriamente (alrededor de seis meses).

6) El plombaje extrapleural aumenta el peligro de la fístula broncopleural después de la resección de éste, y se recomienda que el plombaje sea extraido y que se haga la toracoplastía antes de prosegirse con la resección. Los casos que se efectúen con éxito en la resección bajo el plombaje extrapleural no necesitarán la extracción del plombaje ni la toracoplastía.

RESUME

1) La pneumolyse extra-pleurale peut amener la guérison de la tuberculose dans une proportion importante de cas.

2) Le principal reproche qu'on peut lui opposer est fonction des facteurs anatomiques et anatomo-pathologiques.

3) Pour éviter les complications dues à une fistule broncho-extra-pleurale précoce, il faut faire un examen radiologique précis, avec tomographies, pour exclure les cavités géantes ou superficielles.

4) Si au cours du décollement extra-pleural, on rencontre des adhérences très serrées, il faut interrompre l'opération et ne pas tenter de la pratiquer de force.

5) Pour éviter les risques d'une fistule broncho-extra-pleurale tardive, l'opération doit être considérées dans tous les cas comme un procédé temporaire de collapsothérapie et une thoracoplastie suffisante pour effondrer l'espace doit être réalisée aussi vite que l'extra-pleural est stabilisé (environ six mois).

6) L'introduction d'une substance de plombage dans la cavité extra-pleurale augmente le danger d'une fistule bronchique lors-

qu'on est amené à faire une exérèse sous cet extra-pleural. Les auteurs recommandent que la substance de plombage soit retirée et que la thoracoplastie soit faite avant de pratiquer l'exérèse. Dans les cas pour lesquels l'exérèse a été réalisée avec succès sous le plombage extra-pleural, il n'est pas nécessaire de retirer la substance de plombage et de pratiquer une thoracoplastie.

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Histoplasmin Sensitivity and Pulmonary Calcifications Among 1,000 Residents of the Isthmus of Panama

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Between December 1905 and August 1906, Dr. Samuel Taylor Darling encountered at autopsy at the Board of Health Laboratory, Ancon, Canal Zone, three cases of a previously undescribed parasitic disease which he named histoplasmosis.[1] During the intervening decades, in spite of a high index of suspicion on the part of local clinicians and pathologists, no additional human case has been recognized. The patients described by Darling were immigrant, and there has been justifiable doubt as to whether the fungus, *Histoplasma capsulatum*, had become established on the Isthmus, even though an autochthonous canine infection was reported in 1945.[2] The prolonged absence of recognized human cases of histoplasmosis in an area in which the causative fungus had certainly been present was a paradox inviting study.

In October 1949, an investigation was begun designed to clarify this situation, and a preliminary report on 500 patients has already appeared.[3] These results did not differ significantly from those found in analyzing the final material on 1,000 patients,[4] and may be briefly summarized as follows: Histoplasmin and coccidioidin, in dilutions of 1:100, produced intradermal induration five or more millimeters in diameter (positive test) in 38.7 and 0.8 per cent respectively of the sample tested. Injections of 0.0005 milligram of purified protein derivative elicited positive reactions in 61.3 per cent. The coccidioidin tests served as an adequate *control*,[5] and will not be referred to hereafter. Sex, race and geographic background (see Reference 4 for details) did not appear to effect the prevalence of sensitivity to histoplasmin in this population, but age was a significant factor. Cumulative prevalence-age curves started at zero (newborn infants) and rose sharply during the second, third and fourth decades with gradual leveling off thereafter. It was concluded that these data pointed to some environmental antigenic stimulus but were not sufficient definitely to incriminate *Histoplasma*, and the nature of other, non-specific stimuli was obscure; both factors may have been in operation.

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Other methods of attack on the problem included serologic tests for humoral antibodies (none of which showed significant titers), attempts to demonstrate the fungus itself by microscopic and cultural studies (all of which were negative), and finally, by chest roentgenography. The search for calcific foci in histoplasmin-positive, tuberculin-negative patients yielded provocative results and it is the purpose of this report to describe the findings obtained and to discuss their implications as to the present status of *Histoplasma capsulatum* on the Isthmus of Panama.

Experimental Method and Results

An attempt was made to study 1,000 consecutive admissions for all causes to the "non-white" section of Colon Hospital, Cristobal, Canal Zone. There were 535 males, 465 females. By racial derivation, all but 24 were of Negro or mestizo antecedents. Six hundred and thirty-four had never been away from the Isthmus and none had been to the United States. In addition to indicated diagnostic and therapeutic measures for the present illness, each patient was tested intradermally with histoplasmin and tuberculin. These were performed and read by the writer between 40 and 48 hours later,

TABLE I

Prevalence of Histoplasmin and Tuberculin Sensitivities Among 1,000 Patients, by Age and Sex

Age in Years	Histoplasmin		Tuberculin		Histoplasmin and Tuberculin		Non-reactors		Total
	M	F	M	F	M	F	M	F	
0- 4*	1	1	2	6	-	-	98	79	187
5- 9	2	-	8	6	-	-	17	10	43
10-14	2	5	3	3	1	1	8	6	29
15-19	-	5	1	10	3	3	2	4	28
20-24	4	14	9	24	16	16	3	10	96
25-29	3	8	15	18	21	26	2	9	102
30-34	3	5	18	16	18	22	2	4	88
35-39	1	5	23	21	32	24	3	4	113
40-49	2	3	23	13	34	8	4	5	92
50-59	3	4	20	11	31	13	4	6	92
60-69	3	1	29	14	28	8	14	7	104
70-79	2	-	5	3	3	2	6	2	23
80-89	-	-	2	-	-	-	1	-	3
All Ages	26	51	158	145	187	123	164	146	1,000

*Including 37 newborn infants.

standards being those ordinarily used in interpreting the tuberculin reaction, with the results summarized in Table I.

A 14 by 17 inch teleroentgenogram of the chest was taken on each patient, except for a group of 37 newborn infants. These films were first read by Dr. J. W. Wilkerson, Chief of Medicine, Colon Hospital, with particular reference to active intrathoracic disease. At the end of the study roentgenograms on all patients were reviewed by the writer with regard to the presence of single or multiple pulmonary calcifications,[6-9] using the criterion of High, Zwerling and Furcolow[10] for the latter (*e.g.*, at least five separate

TABLE II

Number and X-ray Distribution of Calcific Pulmonary Lesions Found in 113 Patients, by Intradermal Sensitivities

	INTRADERMAL TEST RESULTS				
	H plus T O	H O T plus	H plus T plus	H O T O	Totals
Total Number Patients in Group	77	303	310	310	1,000
Number of Lesions:					
1	6	15	34	6	61
2	3	10	13	2	28
3	1	5	5	2	13
4-5	-	1	1	1	3
6-7	-	2	-	1	3
8-9	1	-	-	1	2
10-19	1*	-	1	1	3
20+	-	-	-	-	0
TOTAL	12	33	54	14	113
One Lesion Only:					
Parenchymal	3	8	32	4	47
Hilar	3	7	2	2	14
More Than One Lesion:					
Parenchymal	2	12	9	5	28
Hilar	1	2	3	-	6
Hilar and Parenchymal	3	4	8	3	18
Unilateral	*3*	*14*	*12*	*2*	*31*
Bilateral	*3*	*4*	*8*	*6*	*21*
TOTAL	12	33	54	14	113

*Patient with "*Candida* asthma."

areas of calcification in each lung field). In both series of readings intradermal test results were undisclosed. For purposes of analysis the 37 infants were arbitrarily considered roentgenologically negative. The location and number of lesions seen have been tabulated according to intradermal sensitivity in Table II. Nineteen lesions had the so-called "mulberry" configuration but no miliary calcinosis was seen.[10]

The prevalence of calcification in each of the four categories of intradermal responses is shown in Table III. The over-all prevalence was 11.3 per cent. The histoplasmin reactors showed 16 per cent with calcification, as compared with 11 per cent for tuberculin reactors. The group responding to both antigens had a similar rate, 17 per cent. The low prevalence of calcifications among non-reactors (4.5 per cent) was believed to be significantly less than the others.

Table III also gives the proportional distribution of 113 patients with pulmonary calcification by intradermal sensitivity groups. Of those showing calcification, 11 per cent reacted to histoplasmin, 29 per cent to tuberculin, 47 per cent to both antigens and 12 per cent to neither. Calcific foci were seen in patients in the second through the eighth decades of life but study of age-specific prevalences did not disclose definite trends.

Three patients were classified as having "multiple pulmonary calcifications."[10] One of these reacted to both antigens, one to neither, and one to histoplasmin only. The first two gave no reliable history of antecedent pulmonary illness,[9] but the third suffered from long-standing respiratory tract disease characterized by intermittent fever, productive cough, and severe asthma (see Figure 1). She was studied in detail and was found consistently to give pure cultures for *Candida albicans* from sputum

TABLE III

Prevalence of Pulmonary Calcifications Among 1,000 Patients Tested with Histoplasmin and Tuberculin

Antigens	Reactors Among 1,000 Patients		With Calcification		Percentage of Reactors Among 113 Patients with Calcifications
	No.	Per cent	No.	Per cent	
Histoplasmin Only	77	7.7	12	15.6	10.6
Tuberculin Only	303	30.3	33	10.9	29.2
Histoplasmin and Tuberculin	310	31.0	54	17.4	47.8
Non-reactors	310	31.0	14	4.5	12.4
TOTALS	1,000	100.0	113	11.3	100.0

and gastric lavage specimens, together with negative cultural and animal inoculation studies for *Mycobacterium tuberculosis;* "*Candida* asthma" has been reported before.[13]

Discussion

During recent years there has been an upsurge of interest in fungous pulmonary diseases not only in the United States, but throughout the entire hemisphere. According to the available literature, cases of human histoplasmosis have now been found south of the United States, as follows: Mexico,[14] Honduras,[15] Colombia-Venezuela,[16] Brazil,[17] Uruguay,[18] Argentina,[19] and in the Canal Zone.[1] In many areas of Latin America studies of the prevalence of intradermal sensitivity to histoplasmin have been carried out.[4,20-30] When roentgenologic evidence of pulmonary calcific lesions was sought, the definite occurrence of single or multiple calcific foci in tuberculin-negative, histoplasmin-positive individuals was found.[20-24]

On the Isthmus of Panama, geographic hub of the Americas, *Histoplasma* is known to have caused three fatal human infections.

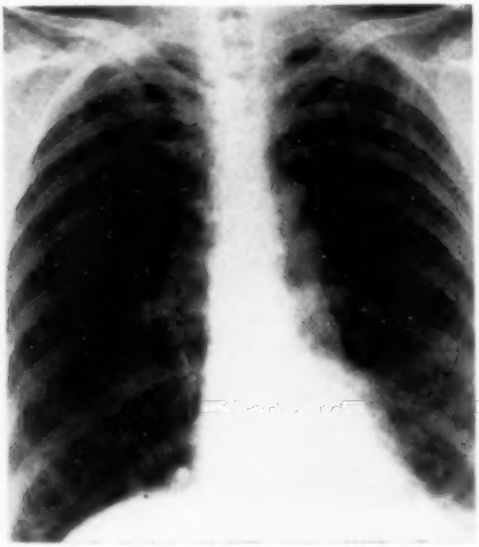

FIGURE 1: Chest roentgenogram of 52 year old Costa Rican woman with "*Candida* asthma" (see text), showing several types of calcific lesions. The "halo" configuration of the right upper lobe lesion has been frequently[11] but not invariably[12] associated with histoplasmosis. A "mulberry" type focus may be seen at the right pericardiophrenic angle and several tiny scattered flecks are present in the left hilar region.

all within a 10 month span near the beginning of the century. During the ensuing 45 years there have been approximately 800,000 admissions to Colon and Gorgas (formerly Ancon) Hospitals for all causes. Over 18,600 autopsies have been done during that time and thousands of gross and microscopic examinations of surgical pathologic specimens have been carried out, but no additional human case has been found. Nevertheless, nearly two-fifths of the 1,000 patients in this study were sensitive to histoplasmin! As was mentioned previously, consideration of these results alone did not appear to clarify the problem: so high a prevalence seemed to reflect on the specificity of the intradermal test itself.

It was felt that analysis of the prevalence of pulmonary calcific foci in relation to intradermal sensitivity might throw additional light on this situation. Although "pulmonary calcifications are apparently nonspecific reactions to a variety of organisms,"[31] it has been well documented that *Histoplasma* may be the causative agent in many instances.[8,10,32] The data here presented have shown that among patients in this region sensitized to histoplasmin, pulmonary calcific lesions occur as frequently as in those reacting to tuberculin, and three times as often as in patients reacting to neither antigen. Even though the foci in these patients cannot be considered conclusive evidence of prior infection with the fungus, taken together with the high prevalence of histoplasmin sensitivity and the similar findings of other workers throughout the Americas where histoplasmosis has been found in recent years, the sum of the circumstantial evidence would support the contention that histoplasmosis does occur on the Isthmus of Panama, apparently in the "benign," subclinical form. These data do not in themselves prove the existence of *Histoplasma capsulatum* here but suggest that further search may disclose additional human cases in the future.

Addendum

Two days after submitting this paper the writer was called to the laboratory to examine a lymph node smear made at the time of autopsy on a four-month old Panamanian, a native of Chilibre, R. de P. Morphologically typical tissue-phase *Histoplasma capsulatum* were seen. Cultural and animal inoculation studies were unsatisfactory. This case, the first in 45 years, supports nicely the prediction made in the text that additional cases might well be found in the future.[33]

SUMMARY

Histoplasmin and tuberculin tests and chest roentgenograms were obtained on 1,000 patients at Colon Hospital, Panama Canal

Zone. Seventy-seven reacted to histoplasmin only, 303 to tuberculin, 310 to both antigens and 310 to neither. Intradermal sensitization increased in prevalence with age. Calcific pulmonary lesions were seen in 113 roentgenograms. Reactors to one or both antigens showed prevalences of calcified foci ranging from 11 to 17 per cent, whereas patients reacting to neither had a significantly lower rate (4.5 per cent). One histoplasmin reactor with bilateral pulmonary calcifications incidentally represented the second published instance of "*Candida* asthma."

Although no human case of histoplasmosis has been recognized in this region since 1906, the findings here reported were interpreted as suggestive circumstantial evidence in favor of the occurrence of non-fatal or "benign" histoplasmosis on the Isthmus of Panama.

RESUMEN

En 1,000 pacientes del Hospital de Colón en la Zona del Canal de Panamá fueron efectuadas pruebas de histoplasmina, tuberculina y roentgenogramas del tórax. Setenta y siete reaccionaron a la histoplasmina solamente, 303 a la tuberculina, 310 a ambas y 310 a ninguna de ellas. La sensibilidad intradérmica aumenta de acuerdo con la edad. Fueron vistas lesiones calcificadas en 113 roentgenogramas. Entre los que reaccionaron a uno o a ambos de los antigenos se encontró una frecuencia de focos calcificados de 11 a 17 por ciento, en tanto que los pacientes que no reaccionaron a ninguno de ellos tuvieron un promedio bajo muy significativo (4.5 por ciento). Un reactor hacia la histoplasmina con calcificaciones pulmonares bilaterales incidentalmente presentó el segundo caso publicado de "asma causada por cándida."

A pesar de que no se ha encontrado ningún caso humano de histoplasmosis en esta región desde 1906, los descubrimientos que aquí se refieren fueron interpretados como evidencia circunstancial de la presencia de histoplasmosis no fatal o benigna en el Istmo de Panamá.

RESUME

L'auteur à pu pratiquer chez 1,000 malades de l'Hôpital Colon (Zone du canal de Panama); l'examen radiologique du thorax et la recherche des tests à l'histoplasmine et à la tuberculine. 77 malades n'étaient sensibles qu'à l'histoplasmine, 303 à la tuberculine, 310 aux deux antigènes, et 310 à aucun d'entre eux. La sensibilité intradermique croit en fréquence avec l'âge. Des calcifications étaient visibles sur 113 radiographies pulmonaires. Alors que 11 à 17% des individus allergiques à l'un ou aux deux antigènes présentaient des calcifications, il n'y a que 4.5% des malades qui n'étaient sensibles à aucun des deux antigènes, chez lesquels cette

constatation put être faite. Un des malades sensible à l'histoplasmine, chez qui existaient des calcifications pulmonaires bilatérales, était atteint d' "asthme blanc." C'est le second exemple connu de cette affection.

Bien qu'il n'y ait pas eu de cas humain d'histoplasmose dans cette région depuis 1906, l'auteur interprète ces constatations comme la preuve certaine qu'il existe dans l'isthme de Panama des cas bénins d'histoplasmose.

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Avascularity of Tuberculous Lesions*

A Major Problem in Therapy

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Introduction

Since the early reports of Feldman, Hinshaw, Karlson and Mann it has been generally accepted that streptomycin is capable of exerting a powerful effect upon the course of a tuberculous infection. The prompt apparent recovery of many forms of tuberculosis, and the, at least temporary, life-saving effect in the fatal forms brought enthusiasm for the new antibiotic. Yet, within a few years, many limitations to the use of streptomycin have been recognized. It has failed to clear the majority of cases of tuberculosis. Treated cases have frequently relapsed within a few months. Continued use of streptomycin caused micro-organisms to become resistant in a high percentage of cases. It has frequently produced symptoms of toxicity when used in more than one gram daily doses. In short, streptomycin can rarely be counted upon to cure tuberculosis.

These limitations were rather surprising and disappointing after it had been determined that streptomycin was tuberculostatic in concentrations that were easily attained as blood and tissue levels. It appeared that there must be some barrier which prevented the penetration of the antibiotic in therapeutic concentrations into the tuberculous lesions.

Since streptomycin has produced, at least temporary, excellent results in early acute tuberculosis, miliary disease, thin-walled cavities, and in other lesions in which the blood supply remains relatively good, but undependable results in chronic fibro-caseous and fibro-cavernous tuberculosis in which the blood supply is relatively poor, it appears that its effectiveness is directly in proportion to the blood supply to the lesion.

Avascularity of Tuberculous Lesions

Pathologists and phthisiologists have recognized that many tuberculous lesions, from tubercle to chronic far-advanced disease, are avascular. Recently observers have realized that avascularity of tuberculous lesions is the definite barrier to chemotherapy.

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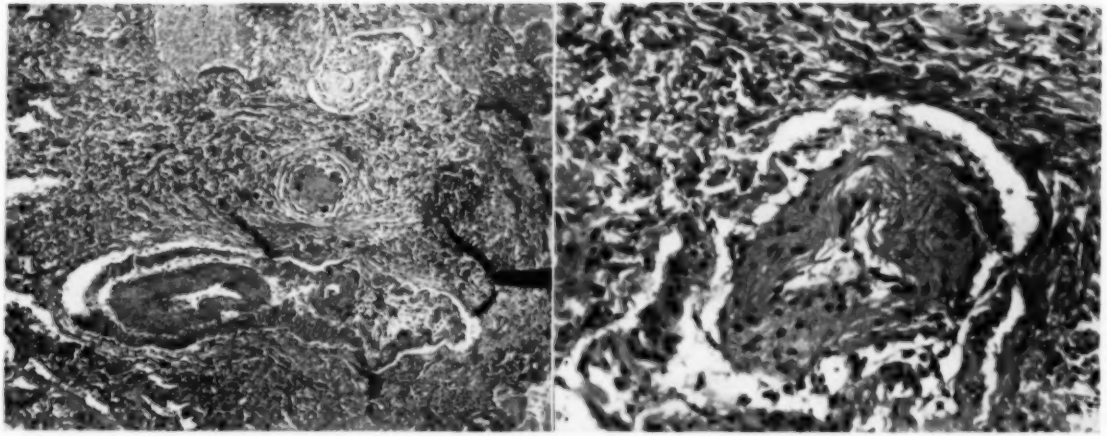

FIGURE 1 FIGURE 2

Figure 1: Microphotograph (low power) of a section taken from the wall of a tuberculous cavity, showing several vessels which are thickened almost to the point of occlusion.—*Figure 2:* Microphotograph (high power) of the same section taken from the wall of a tuberculous cavity (Figure 1), showing the thickened and fibrotic wall of a blood vessel. The lumen is nearly occluded and contains no evidence of blood cells. (Microphotographs by Armed Forces Institute of Pathology).

Birkelo and Brosius[1] have demonstrated by roentgen visualization of radiopaque injections into the pulmonary arterial tree (autopsy material) that chronic tuberculosis causes a marked reduction in the size of the large trunks, abrupt terminations of the medium size arteries and complete obliteration of the fine branches. Others[2,3] have reached the same conclusion by means of angiocardiography.

Pathologic studies of the pulmonary arteries within tuberculous lesions frequently show extensive thromboses, which begin in the terminal branches and spread to the large trunks; the vessel walls become thickened and fibrotic, and the lumina may become completely occluded by endarteritis obliterans[4,5] (Figures 1 and 2).

Ischemic (caseous) necrosis is frequently associated with endarteritis. The involved areas are usually surrounded with fibrosis. As the disease progresses, the avascularity, the necrosis and the fibrosis become more and more complete. These pathological changes constitute a definite barrier which not only interferes with the nutrition of the involved areas, but also impedes or prevents antibiotics from reaching the tubercle bacilli.

Streptomycin—Tuberculostatic and Tuberculocidal

For several years it has been generally accepted that streptomycin is actively tuberculostatic. Recently, it has been demonstrated that it is also tuberculocidal[6] at blood and tissue levels which are easily attained. These observations further substantiate the original work of Waksman, et al.

While it has been a simple matter to obtain therapeutic levels of streptomycin in normal vessels and tissues, it has been difficult to attain these levels within avascular, necrotic, and fibrotic lesions of tuberculosis. Yet, to permit these levels of streptomycin to fall below therapeutic concentrations within tuberculous lesions, insures the failure of the antibiotic to produce its desired tuberculostatic and tuberculocidal actions, and invites the emergence of resistant tubercle bacilli. While Medlar, Bernstein, and Reeves have shown that streptomycin can penetrate both the solid necrotic lesions and the walls of cavities, the fact that a higher proportion of the bacterial population were resistant within these lesions, and resistant to a higher degree than in other lesions, indicates that streptomycin can penetrate the pathological barriers, but not in therapeutic concentrations.

Shamaskin, Des Autels, Sweany and Zvetina[7] have made the following important statement: "Until another and more effective antibiotic against tuberculosis is discovered, we should change our mode of attack on this problem, and aim our efforts primarily at finding means of penetrating more effectively the defenses

behind which the tubercle bacilli may find protection in the human body. We must enable the drug to make adequate contact with the (micro) organism wherever it may be. It does not seem likely that the conditions which seem to prevent the drug from entering the caseo-necrotic mass in therapeutic concentrations, could be overcome with relative safety by sheer volume of antibiotic."

Attempts to Penetrate Vascular Barriers

Several observers are exploring the various methods of penetrating vascular barriers. Cavernostomy[8] is being used to drain cavities and to place a therapeutic agent directly within the cavity. Potassium iodide,[9] antihistaminic agents,[10] detergents,[11] and streptokinase[12] are being used in association with antibiotics in an attempt to soften or liquify the tuberculous lesion in order to allow the antibiotic to become more effective. Tuberculin[13-16] is being used in an attempt to revascularize tuberculous lesions. This is thought to permit a greater penetration of the therapeutic agents into the tuberculous lesions, and also allows the liberation of micro-organisms from the lesion into the blood stream so that they can be exposed to therapeutic concentrations of antibiotic agents.

Preliminary reports indicate that each one of the above mentioned attempts to penetrate the pathological barriers of chronic tuberculous lesions, has produced more effective results than experienced when the antibiotic is used alone. It presently appears that a positive effort must be made to penetrate these barriers if the full effectiveness of present and future antibiotic and chemotherapeutic agents is to be obtained in chronic tuberculosis.

SUMMARY

The extensive thrombosis and obliterative endarteritis of vessels entering chronic tuberculous areas of disease produce essentially avascular lesions. Other closely associated pathological changes, ischemic (caseous) necrosis and fibrosis, further increase the avascularity. There is some evidence that streptomycin penetrates these pathological barriers; however, when it enters in less than therapeutic concentrations, it is neither tuberculostatic nor tuberculocidal, and the emergence of resistant tubercle bacilli results.

Efforts are presently being made to penetrate pathological barriers by various methods so as to allow drugs to come into direct contact with tubercle bacilli. The following methods have been tried: cavernostomy, potassium iodide, antihistaminics, detergents, streptokinase and tuberculin. Of these, tuberculin appears to revascularize tuberculous lesions, exposing tubercle bacilli to therapeutic levels of chemotherapeutic agents.

It appears that further effort must be made to penetrate pathological barriers of chronic tuberculosis, if the full effectiveness of present and future chemotherapeutic agents is to be obtained.

RESUMEN

La extensa trombosis y la arteritis obliterante de los vasos que entran en las areas de la enfermedad crónica tuberculosa, producen esencialmente lesiones avasculares. Otros cambios patológicos estrechamente asociados, come l anecrosis isquémica (caseificación) y fibrosis, aumentan aún la avascularidad. Hay alguna evidencia de que la estreptomicina penetra a través de estas barreras patológicas; sin embargo, cuando entra, lo hace en concentraciones inferiores a las terapéuticas; no es entonces ni tuberculostática ni tuberculicida y resulta la aparición de bacilos resistentes.

Se estan haciendo esfuerzos para lograr penetrar las barreras por varios métodos de manera que se logre que la droga llegue a contacto directo con los bacilos tuberculosos. Los siguientes métodos se han ensayado: cavernostomía, yoduro de potasio, antihistamínicos, detergentes, estreptoquinasa y tuberculina. De estos la tuberculina parece lograr la revascularización de las lesiones tuberculosas, exponiendo el bacilo tuberculoso a las concentraciones terapéuticas de los agentes chimioterápicos.

Parece que se deben hacer ulteriores esfuerzos para penetrar las barreras patológicas de la tuberculosis crónica si hay que obtener una efectividad completa de los presentes y futuros agentes quimio-terápicos.

RESUME

La thrombose extensive et l'endartérite oblitérante des vaisseaux qui sont situés dans les zones de tuberculose chronique expliquent que les lésions soient essentiellement avasculaires. Cette particularité est encore accrue ultérieurement par l'association d'autres altérations, la nécrose ischiemique (caséeuse) et la fibrose. Il semble bien que la streptomycine puisse pénétrer malgré ces obstacles. Cependant, lorsqu'elle pénètre à une concentration infrathérapeutique, elle n'est ni tuberculostatique, ni tuberculicide, et il en résulte l'apparition de germes streptomycino-résistants.

Actuellement, des efforts sont faits pour faire pénétrer la drogue à travers ces obstacles, et lui permettre d'entrer directement en contact avec les bacilles tuberculeux. On a essayé les méthodes suivantes: cavernostomie, iodure de potassium, antihistaminiques, détergents, streptokinase et tuberculine. Parmi ceux-ci, la tuberculine semble rétablir la vascularisation des lésions tuberculeuses, et permet de faire pénétrer jusqu'au bacille des doses thérapeutiques suffisantes.

Il semble que de nouveaux efforts doivent être faits pour que puisse pénétrer, à travers les barrières anatomo-pathologiques qui se constituent dans la tuberculose chronique, les agents chimiothérapiques actuels, et ceux qui pourraient être utilisés dans l'avenir. C'est ainsi qu'on obtiendra leur efficacité maximum.

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The Early Recognition and Treatment of Bronchogenic Carcinoma*

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Carcinoma of the lung is a formidable problem in medical practice. In the past few years it has become the most frequent malignancy.[1]

Bronchogenic carcinoma often gives a clue to its early existence by simple radiographic technique, yet delayed diagnosis is all too frequent. Procrastination on the part of the patient with symptoms and by the referring physician, and extensive diagnostic studies all contribute to the delay before the patient is considered for surgery.[2,3] Added to this period of "watchful waiting," which can be more or less measured in time, is that silent asymptomatic phase of the tumor whose duration can not be estimated.[4] It is not surprising, therefore, that in the institutions with large series of cases, most patients are admitted in an inoperable condition.[1,3,5,6]

It is not the purpose of this paper to discuss the symptoms, signs, and course of bronchogenic carcinoma as the clinical picture has been well published.[1-8] Suffice it to say that this condition simulates many pulmonary disorders, thus, cancer of the lung should be given first consideration whenever one is confronted with an unexplained pulmonary lesion.

Analysis of Cases

Seventy consecutive patients admitted with bronchogenic carcinoma were studied. Of these, only 20 were deemed to be operable (Table I). Criteria for inoperability included rib or other bony metastases, involvement of the trachea as observed on bronchoscopy, recurrent laryngeal nerve palsy, pleural fluid containing

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tumor cells, vena caval obstruction, clinical evidences of lymphatic or other distant metastases, and advanced cachexia due to malignancy. One patient with Lutembacher's syndrome with cytologic proof of bronchial cancer was regarded as unsuitable for surgery.

Ten of the 20 operated cases were found to be resectable. Of those resected, five are still alive with an average of 17 months from the earliest clinical manifestation of their disease. The remainder died, averaging eight months from the earliest evidence of their illness. This last figure is little different from that en-

TABLE I

Total Number of Cases		70	
Number Operated		20	
Resectable — 10		Non-Resectable — 10	
Still Living — 5 (Av. 17 mos.)		Still Living — 1 (18 mos.)	
Dead — 5 (Av. 8 mos.)		Dead — 9 (Av. 11 mos.)	
Number Not Operated			
Diagnosis not made	— 1	Still Living	— 8 (Av. 18 mos.)
Refused Surgery	— 1	Dead	— 41 (Av. 11 mos.)
Inoperable	— 48	No Follow-up	— 1

TABLE II: Morphologic Types

Non-Resectable		Resectable	
Squamous Cell	— 4	Squamous Cell	— 5
Adenocarcinoma	— 2	Undifferentiated	— 2
Undifferentiated	— 2	Aleveolar Cell	— 1
Type Unknown	— 2	Type Unknown	— 2

Prognostic Significance of Cytology in Bronchogenic Carcinoma

TABLE III

Total Number of Cases		70
Bronchoscopic Examinations		47
Bronchoscopic Biopsies		15 (12 Patients)
Living	— 5 (Av. 17 mos.)	
Dead	— 6 (Av. 15 mos.)	
No Follow-up	— 1	
Tumor Diagnosis Made on Bronchoscopy		25
Tumor Diagnosis Made on Cytologic Examination of Secretions		8
Tumor Diagnosis Made on Biopsy of Visible Lesion		10

TABLE IV

Total Number with Chronic Pulmonary Disease		19
Tuberculosis	— 7	
Bronchial Asthma	— 5	
Chronic Bronchitis	— 6	
Pulmonary Emphysema	— 1	

countered in the group of nine dead with non-resectable tumors and in the group of 41 dead with inoperable carcinoma.

An attempt was made to assess the prognostic significance of cytology in the 10 operated patients. The morphologic types found in the resectable and non-resectable groups are listed in Table II. From this brief number it is impossible to draw any definite conclusions, but it can be seen that no definite trend was present.

Forty-seven bronchoscopies were performed. Fifteen biopsies of visible lesions were taken in 12 patients (Table III). It can be seen that the subsequent course of the biopsied cases was not materially different from that of the entire series.

Diagnosis was made on direct inspection through the bronchoscope in 25 cases, or in 53 per cent of the total number of examinations. In 10 of these, bronchial biopsy confirmed the impression of carcinoma. In eight instances positive diagnosis was made on cytologic examination of secretions obtained at bronchoscopy. In four of these cases the examiner could not visualize any tumor tissue. This brought the figure to 63 per cent of all bronchoscopies.

Nineteen of the 70 patients with bronchogenic carcinoma were found to have coexistent chronic pulmonary disease (Table IV). This number included seven with pulmonary tuberculosis, five with bronchial asthma, six with chronic bronchitis, and one with chronic diffuse obstructive emphysema. Each patient with bronchial asthma and with chronic bronchitis was classed as such when there was symptomatology referrable to these conditions of over five years duration. Bilateral physical signs were present in each patient included in this series as having bronchial asthma.

During the period in which the 70 patients with bronchogenic carcinoma were admitted, only 23 cases of gastric carcinoma were similarly hospitalized.

Illustrative Cases

Case 9: C.E., male, white, 69 years old, had noted cough with hemoptysis for three weeks. There was also exertional dyspnea of 20 years duration. Physical examination, substantiated by radiographic studies (Figure 1), resulted in a diagnosis of Lutembacher's syndrome. Bronchoscopy revealed a bleeding tumor mass in the right lower lobe bronchus. This could not be biopsied, but cytologic examination of bronchial secretions revealed definite evidence of squamous cell carcinoma. He was deemed inoperable because of the cardiac status. He was digitalized and sent home.

The marked hilar enlargements in this syndrome are well known and in this instance the radiographic appearance masked the presence of the tumor.

Case 13: D.K.McD., male, white 52 years old, underwent a hemorrhoidectomy 20 months previously. Routine roentgenogram of the chest showed a lesion in the left lung field which was unfortunately overlooked.

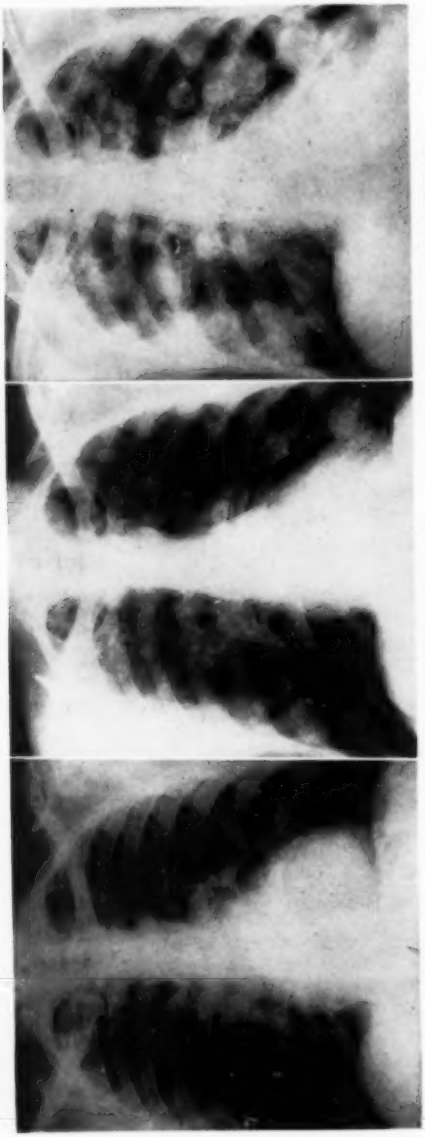

FIGURE 5b

FIGURE 5a

FIGURE 4

He was readmitted with a left sided chest pain (Figure 2). After diagnostic studies surgery was recommended, but the veteran refused. The diagnosis was confirmed several months later on autopsy.

Case 21: V.A.S., male, white, 51 years old, was admitted with cough and chest pain of one years duration. Radiograph of the chest demonstrated a right paramediastinal density (Figure 3a). At bronchoscopy a carcinoma in the right upper lobe bronchus was visualized. Pneumonectomy was performed. Aside from a postoperative bronchopleural fistula (Figure 3b), which was successfully managed, the patient has done well and is still alive, four years later.

A mass apparently close to the mediastinum is thus not necessarily a barrier to a successful outcome.

Case 24: W.S., male, white, 41 years old, gave a history of chronic productive cough of seven years duration and right chest pain, hemoptysis, and night sweats of three weeks duration. Chest x-ray film revealed a

FIGURE 1

FIGURE 2

FIGURE 3a

FIGURE 3b

small peripheral density with a prominent hilum on the right side (Figure 4). A week later there was a small infiltration in the right first interspace. Extensive and protracted diagnostic studies were not remarkable. A gradual increase in size of the nodular density prompted exploration five months after admission. An inoperable carcinoma was found.

Extensive diagnostic studies contributed to confusion and delay in a situation where early exploration, in retrospect, was clearly indicated.

Case 25: E.H., male, white, 45 years old, was admitted with productive cough and weight loss. Roentgenogram of the chest was interpreted as metastatic carcinoma (Figure 5a). Biopsy of a neck mass revealed an epidermoid carcinoma. After a downhill course (Figure 5b) post-mortem examination disclosed a bronchogenic carcinoma, left lower lobe bronchus, with metastases to both lungs, and old tuberculosis at the right apex with bilateral miliary dissemination. This was a bronchogenic car-

FIGURE 6a

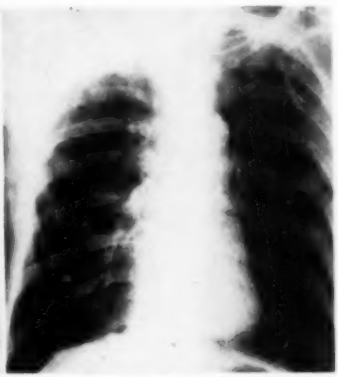

FIGURE 6b

FIGURE 7a

FIGURE 7b

cinoma that masqueraded as a bilateral metastic pulmonary tumor. The exacerbation of the old tuberculous process may have been incident to the cachexia or to erosion by tumor. It is conceivable that lymphatic blockage by tumor may favor hematogenous dissemination of tubercle bacilli.

Case 43: C.A.C., male, white, 63 years old, was admitted for chronic alcoholism and lues. Routine chest x-ray film (Figure 6a) was diagnosed as fibrosis at both apices, with bullous emphysema at the right apex. The patient was admitted one year later with an inoperable Pancoast tumor (Figure 6b) on the right, confirmed by autopsy later.

The localized bullous emphysema, in retrospect, was evidently secondary to a partial bronchial occlusion. Recognition of this possibility might have led to early exploration of this patient's chest.

Case 51: R.S., male, white, 61 years old, was admitted because of an incisional hernia following a partial gastrectomy. There was also a history of asthmatic bronchitis of 17 years duration. Roentgenogram of the chest (Figure 7a) was interpreted as showing bilateral emphysema with fibrosis. Five months later the patient was readmitted with fever and increased cough. He was treated for pneumonia (Figure 7b), but pursued a rapidly downhill course. Post-mortem examination revealed an extensive bronchogenic carcinoma.

The coexistence of bronchogenic carcinoma with chronic pulmonary disease will be discussed later in this paper. The symptoms of the latter may mask those of a malignant process in the lung.

Discussion

The majority of patients with bronchogenic carcinoma are either inoperable or non-resectable when diagnosed. Of our entire series, only five individuals, or 7 per cent, are still alive with a chance at cure. This is in general agreement with that reported elsewhere.[5-7] The results of bronchoscopy, reported herein, do not differ materially from those of other investigators.[1,3,6-8] It has been emphasized that with negative bronchoscopy positive diagnosis may be made by supplementing with cytological examination of sputum and secretions. This has been reported[9] to result in high percentages of positive yields. It must be remembered, however, that false positive and false negative results do occur, and that there is great need for adequate training of laboratory men who wish to undertake this time-consuming procedure.

Additional bronchoscopic information of value is the site and extent of the tumor in its relation to the trachea and major bronchi, and evidence of metastases to the mediastinum is shown by widening of the carina or fixation of the bronchi. At bronchoscopy the larynx likewise can be inspected for evidence of recurrent laryngeal nerve involvement.

A correlation between cell type and rate of progression of the

disease has been reported.[6] This could not be demonstrated in the small series of operated cases described above.

It might be supposed that bronchial biopsy may be a factor in enhancing the dissemination of tumor cells as a result of cutting into tumor tissue.[7] Analysis of the subsequent duration of life of the biopsied cases in this series does not bear out this impression.

The frequent coexistence of chronic pulmonary disease with bronchogenic carcinoma, 27 per cent of cases in this report, is of considerable interest. Patients with chronic pulmonary disease require close and careful observation as pulmonary malignancy may be masked by the underlying pathology. The frequent association of bronchial cancer with pulmonary tuberculosis is not surprising when one considers the relative incidence of the two diseases, and the trend of tuberculous morbidity to move into the older age groups.[10] Whether chronic pulmonary infection can predispose to malignancy through metaplasia of the bronchial epithelium is an interesting possibility.

It has been the writers' experience, and that of others,[4] that distant metastases may exist in the absence of pulmonary symptoms, and even where no pulmonary lesion can be demonstrated radiographically. This latter situation is fortunately not common.

Too much valuable time can be lost as a result of subjecting the patient to extensive diagnostic studies. However, if after thorough study, including sputum and tuberculin testing, appropriate x-ray films and bronchoscopy with biopsy and cytologic studies, a pulmonary radiographic density is still unexplained after a period of two weeks, immediate exploration is indicated.

Since most patients with bronchogenic carcinoma reach the surgeon in an inoperable state, a constant search for those in the "silent phase" is necessary. In this stage of bronchial cancer, the tumor may be evident but symptoms are not yet present. Pneumonectomy at this point should be expected to be curative in a far greater proportion of cases than that which occurs today. The need for mass survey films[4,11] has been stressed. It is clear that sole reliance upon symptomatology and accepted diagnostic techniques leave much to be desired.

SUMMARY

1) It is proposed that roentgenograms of the chest be taken on all adult members of the population at six month intervals. This can be done on all healthy individuals, on all hospital admissions, and as part of every pre-employment examination in each industry. Routine chest x-ray films should be performed on all persons seen in the physicians' offices.

2) Since lesions have been overlooked in survey examinations,

it is felt that each survey film should be inspected by two competent physicians, one of whom should be a qualified radiologist. Any differences of opinion could then be mediated by appropriate consultation and studies.

3) Although great advances in the ability to diagnose bronchogenic carcinoma have been made, sole reliance on accepted principles of symptomatology and investigative technique fall far short of the immediate goal of saving the lives of the majority of patients with this condition.

RESUMEN

1) Se propone que se tomen roentgenogramas del torax cada seis meses a todos los adultos de la población. Esto puede hacerse en todos los individuos sanos, en tods los entrados a hospitales, y como parte de todo examen de admisión a empleo en toda industria. Se deben hacer peliculas de rutina en todas las personas vistas en las oficinas de los médicos.

2) Puesto que se han pasado por alto lesiones en algunas investigaciones en grupo, se cree necesario que cada pelicula sea observada por dos médicos competentes, uno de ellos un roentgenólogo calificado. Cualquiera diferencia de opinión puede entonces ser transada por la consulta adecuada y otros estudios.

3) Aunque se han hecho grandes adelantes en el diagnóstico del carcinoma bronquigénico, la confianza en solo los principios aceptados sobre la sintomatología, y técnicas de investigación se quedan muy lejos de bastar para el fin inmediato de salvar las vidas de la mayoría de los enfermos con este padecimiento.

RESUME

1) Les auteurs proposent que des radiographies pulmonaires soient faites pour tous les individus adultes de la population tous les six mois. Ceci peut être exécuté chez tous les individus bien portants, chez tous les individus entrant à l'Hôpital pour une raison ou pour une autre, et en partie dans toutes les entreprises au moment de l'examen d'embauche. De façon systématique, une radiographie pulmonaire doit être faite chez toute personne qui vient consulter un médecin.

2) Depuis que les examens sont utilisés pour la découverte des lésions pulmonaires, les auteurs pensent que chaque examen de film devrait être fait par deux médecins compétents, dont l'un serait un spécialiste en radiologie. Chaque fois qu'il y aurait une interprétation différente entre ces deux examens, il y aurait lieu d'envisager une consultation et des études pour trancher la question.

3) Quoique de grands progrès aient été réalisés dans le diagnostic

du cancer pulmonaire, il ne faut pas se fier sur les principes classiques de la symptomatologie et des méthodes d'investigation si l'on veut sauver la vie de la majorité des malades.

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Contribution of Angiopneumography to Some Problems of Pulmonary Physiopathology*

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At the Eighth Panamerican Meeting of Tuberculosis (México, 1949), it was said: "The comparative analysis of results obtained with both techniques, angiopneumography and bronchospirometry, is worthy of interest."[1]

In a similar way, at the Third Interamerican Meeting of Radiology (Santiago, Chile, 1949) it was established, as proposed by one of us, that angiocardiography may well serve to study pulmonary and circulatory physiology and phisiopathology.[2]

Recently it has been said[3] that "angiocardiography allows to appraise lung functional value through the study of intrapulmonary vascularization."

The present paper deals with 41 angiopneumographic studies made on 37 patients with different pathological lung conditions which, with some exceptions, were of tuberculosis origin. A comparative study between angiopneumography and broncospirometry has been made on 24 patients; in all of them appearance of the pulmonary circulation has been studied.

Comparison Between Angiopneumographic and Bronchospirometric Studies

Materials and Methods: We have intentionally selected different pathological conditions in which we could expect to find a diminished respiratory function. The pathological conditions existing in the aforementioned 24 patients were as follows:

I. thoracoplasty: 2 cases,
II. fibrothorax: 2 cases,
III. pachypleuritis: 6 cases,
IV. partial stenosis of the main bronchus: 1 case,
V. bilateral ulcerative tuberculosis: 4 cases,

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VI. pneumothorax: 7 cases (the stump was radiologically clear in three cases, partially clear in two cases and definitely opaque in two cases),

VII. reexpanded lung (after phrenicoparalysis and not complicated pneumothorax): 1 case,

VIII. ligature of the left branch of the pulmonary artery: 1 case.

We have followed the techniques presented in a former paper.[4*]

Results and Discussion: Within four seconds after the end of the injection, four films are obtained: normally, the main and segmental branches of the pulmonary artery may be seen in the first or second film and their arborizations may be followed up to the peripheral limits of the lung [Figure 1 (2)].

The venous circulation normally appears from the third film on, with more intensity in the last films as the arterial shadows become indistinct; the venous shadows present a characteristic mottling. The main veins may be seen in some cases, more caudally than the arterial main branches [Figure 1 (4)].

Localized modifications of the blood vessel shadows and changes

*Angiocardiography with a ventrodorsal x-ray projection was performed according to the Robb-Steinberg technique, with injection in the arm vein of 40 cc. of 70 per cent solution of the x-ray opaque substance as the standard adult dose.

The numbers in the figures indicate the order of the films in the angiocardiographic series.

In 180 cases studied for different purposes we have not had any important accident.

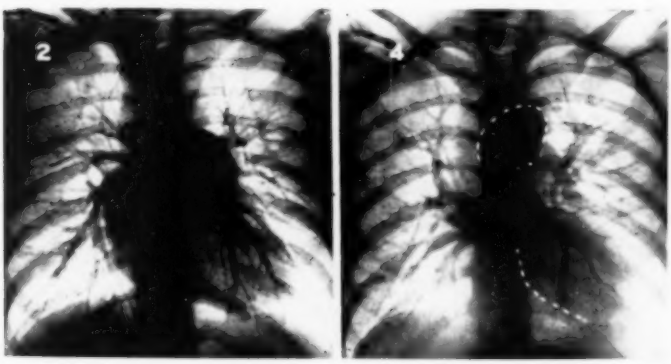

FIGURE 1: Normal angiopneumogram. (2) Note contrast of the right heart cavities and of the arterial pulmonary trunk; one can easily see the two arterial pulmonary branches and the arterial branches of the second, third, fourth and fifth order. (4) One can easily see the venous branches that flow together in the four pulmonary veins, which are in a more caudal plane than the two arterial branches; note also the left heart cavities and the aorta.

in the chronology of their development are seen in these different pathological conditions. Sometimes it is possible to see the reduction, even the complete absence, of vascular contrast in a certain region (Figures 2a and 2b), and in some cases we have observed the complete absence of the circulation of one lung (Figures 3a and 3b). It is also possible in some areas to see well contrasted arterial branches, even in the last films, when the majority of the arterial shadows have been replaced by the venous shadows in normal areas; in these cases the general appearance is similar to the one called "winter tree appearance" in bronchographic study (Figures 4a and 4b). This particular appearance is due to the partial stoppage of the contrasting fluid in some arterial branches, as a result of circulatory impediment localized in the small arborizations.

The bronchospirometric tests were always performed within a few days of the angiopneumographic tests and, in the pneumothorax cases, it was tried to obtain the two tests with the same degree of collapse.

From our researches two important facts stand out which are evident in Figures 3, 4, 5, 6 and 8, some of the more characteristic cases.

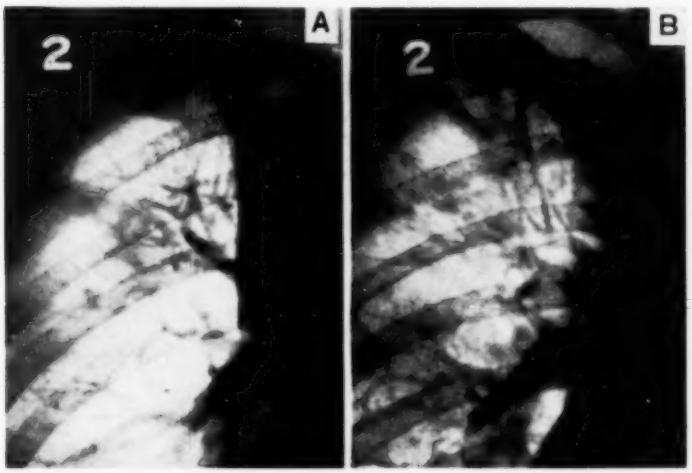

FIGURE 2: (A) Refers to a case of a small cavity of the upper third of the right lung; a decrease of the contrast and an amputation of some vascular branches of the third order can be observed in the area corresponding to the process. (B) Corresponds to a case of a large cavity of the apex of the right lung; decrease of the contrast and amputation of the greatest part of the vascular branches corresponding to the upper third of the right lung can be noticed.

First: *in the areas where the absence, the decrease or the delay of vascular contrast reveal that the circulation is lacking or scarce, there exists a proportional reduction in the oxygen consumption* which is easily explained, it being that the local diminution of the blood flow causes a reduction in the gaseous interchange.

The other fact, different from the first, but closely related to it, is that *in the lung where the respiration (oxygen consumption) is diminished, there always exists a parallel reduction of the circulation*. This last observation helps to decide the debate existing on this problem, improperly called the pulmonary short-circuit (shunt). This problem brings up for discussion the fact of whether it is possible that a functionally important circulation could persist in certain pathological conditions which affect the gaseous interchange of a more or less large area of the lungs. It is clear that if this happened the venous blood passing through this area would arrive at the left heart without being oxigenated and would abnormally decrease the degree of the arterial oxygen saturation.

Many authors still give great importance to this possibility during the course of certain pulmonary diseases; on the contrary, others are opposed to this thesis. In 1934 Bjorkman[5] wrote: "It is probable that a reduction in oxygen consumption, which has been shown bronchospirometrically in almost all unilateral lung conditions, is related to a corresponding reduction in blood circulation in the affected areas, with an increased circulation in the unaffected lung."

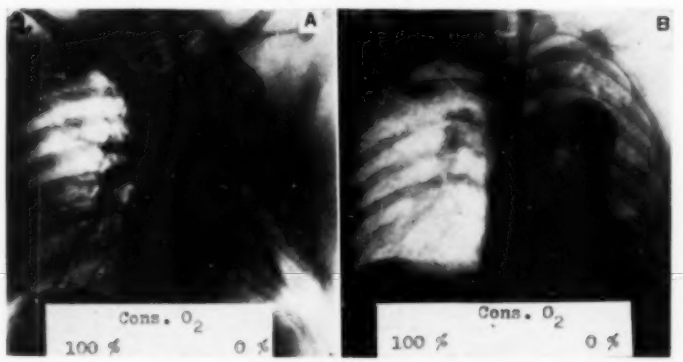

FIGURE 3: (A) Corresponds to a case of left upper thoracoplasty; circulation, evidently increased, is found only in the right lung; in the left thoracoplastied lung no arterial or venous branch is seen. In parallel form oxygen consumption is found only in the right lung. (B) Refers to a case of ulcerated fibrothorax due to pleural effusion; "amputation" of the left branch of the pulmonary artery; increased circulation in the healthy lung. In parallel form oxygen consumption is found only in the right lung.

The veracity of the latter statement arises clearly from our findings. In effect, according to them, *the possibility that appreciable quantities of blood cross some pulmonary zones without being oxygenated is (if it exists) of secondary importance in the pathological conditions studied and probably in all pleuro-pulmonary processes once stabilized.**

In reality the pathological anatomy shows that the processes studied and similar others, have a tendency to reduce the number, the elasticity and the caliber of the pulmonary vessels, in other words, to increase the resistance of the local circulation. If we keep in mind that the possible derivations of the pulmonary circulation are very abundant, we can deduce that any pathological process, parenchymatous or pleural, which causes a small local increase of the vascular resistance in the lung, lobe or segment, forces the blood to deviate in a greater or lesser quantity from the damaged areas towards the healthy areas, where that resistance is less; this easily produces a localized circulatory deficit with a corresponding decrease in oxygen consumption. On the other hand, the local decrease of oxygen absorbtion could produce, reflexly, a deficit of the flow in the damaged area.

From the theoretical viewpoint it is convenient to remember in this respect the studies of von Euler and Liljestrand[6] who experi-

*From this we naturally exclude those processes as arterio-venous aneurysms of the lung, in which a real short-circuit in the parenchyma exists.

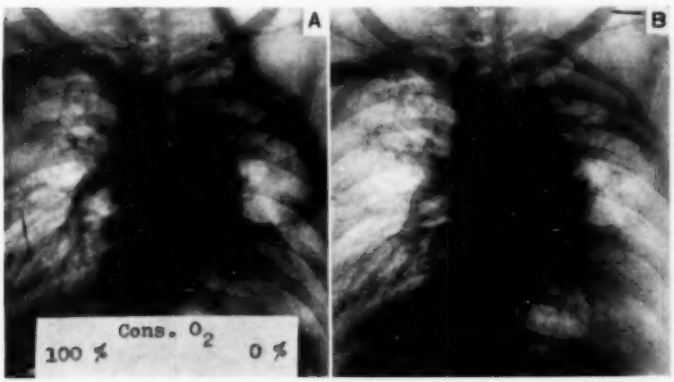

FIGURE 4: Ulcerated cirrhotic pleural and pulmonary process of one half of the left lung. In this lung one only observes the inferior lobular arterial branch, that appears late (**A**) and that maintains its invariable aspect in the rest of the plates (**B**) (sluggish flow). Circulation is essentially found only in the right lung; in parallel form oxygen consumption is only found in the right lung.

mented with cats breathing in an atmosphere of low oxygen concentration and found an increase in the pressure of the pulmonary artery which they attributed to a generalized constriction of the pulmonary vessels due to direct action of the anoxia on the vessel walls.

From the practical viewpoint the question arises as to whether poorly irrigated areas regain their function when circulatory re-

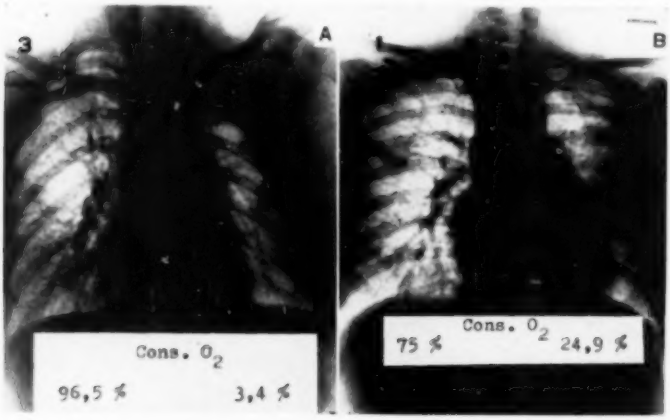

FIGURE 5: Two cases of left postpneumothoracic pachypleuritis. In both cases absence of irrigation is found in the upper half and sluggish circulation in the lower half of the left lung. In a corresponding form the oxygen consumption is very much decreased in the left lung.

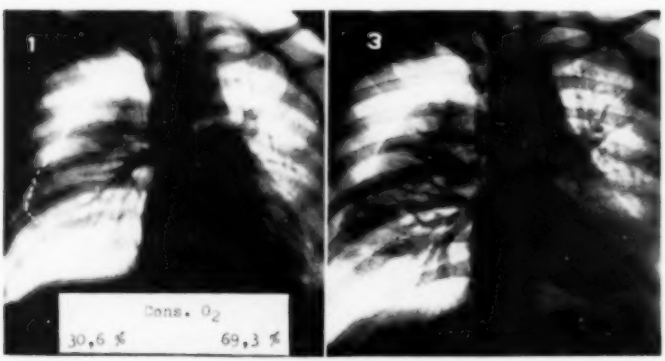

FIGURE 6: Right therapeutic pneumothorax with clear stump. Normal circulation in the left and good arterial (1) and venous (3) circulation in the right stump. In a corresponding form the oxygen consumption is good in the right stump.

sistance increases in formerly healthy or less diseased areas, or when the latter areas have been suppressed by a surgical intervention.

The bronchospirometrical method allows the obtaining of partial data, useful in the study of the respiratory function. It has the advantage of being quantitative, but it also has the inconveniences of being rather bothersome for the patient and of requiring skill on the part of the technician. Some mistakes are also possible.

The angiopneumographic method is apparently qualitative, but allows a global appraisal of the function not only of each lung, but also of each pulmonary segment; besides, it is simple to execute and, consequently, useful in a greater number of cases.*

Angiopneumographic Study in Different Pathological Processes of the Lung[8]

The studied material is distributed in the following way:

I. ulcerative tuberculosis: 4 cases,
II. unilateral pneumothorax: 13 cases,
III. bilateral pneumothorax: 1 case,
IV. re-expansion of the lung after pneumothorax: 8 cases,
V. pachypleuritis: 6 cases,
VI. fibrothorax: 2 cases,
VII. partial stenosis of a main bronchus: 1 case,
VIII. total atelectasis: 5 cases,
IX. pulmonary decortication: 2 cases,

I. *Ulcerative tuberculosis:* We have studied four cases: one with small cavities in both apices, the remaining three with unilateral cavity.

From results obtained in this group of patients, we can deduce that an appreciable decrease of irrigation (even the complete suppression in cases of important or ulcerative lesions) exists in diseased areas of the tuberculous lung (Figures 2a and 2b); this agrees with the observations of Ameuille et al.[9] and of Celis et al.[7]

*While this was being written, we received a paper by Celis et al.[7] and our conclusions agree perfectly with theirs.

We just prefer our technique to the one used by the Mexican authors, who introduce a catheter, through the previously exposed jugular vein, up to the right auricle. Using this method, they naturally obtain less dilution of the opaque substance and, for that reason, better contrast and more perfect radiographies. Thus, a small surgical intervention, which obviously requires to be executed in a specialized centre, is necessary instead of a simple venous puncture.

Any kind of simplification in the technique, any possibility to practice it, without risk, in the greater number of cases, without any particular preparation or special care, is what really matters.

In the healthy areas of the affected lung the circulation is practically normal.

II. *Unilateral pneumothorax:* The study of the pulmonary circulation during pneumothorax has always been of great interest to lung specialists.

The first angiopneumographies, done for practical purposes, were obtained to clarify this problem by L. and A. de Carvalho.[10] They found on four cases the existence of a direct relation between the degree of pulmonary compression and the diminution of the circulation, as well as an increase of the circulation in the healthy lung.

Later, Ameuille et al.[9] observed that the circulation in the compressed stump was delayed and that sometimes it was not possible to find blood vessels in the stump.

Recently, Bourgeois et al.[11] observed in eight cases of pneumothorax an extreme variability in the circulation of the collapsed lung.

Even more recently, L. de Carvalho[12] insists that it is enough to introduce a very small quantity of air into the pleura to produce an important diminution of the circulation. We have studied 13 cases of unilateral pneumothorax, which have maintained in hypotension, with the following characteristics:

a) with a clear stump: 4 cases (Figure 6),
b) with a partially gray stump: 2 cases; one due to atelectasis, the other due to infiltration,
c) with a gray stump: 3 cases; one due to atelectasis, one due to

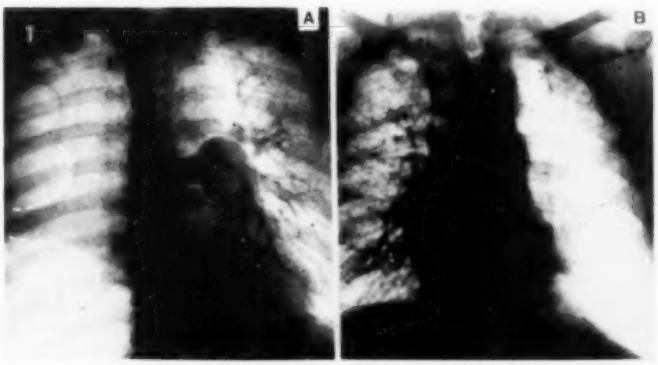

FIGURE 7: (A) Refers to a partial right pneumothorax with pachypleuritis of the stump; complete absence of irrigation in the stump and increased circulation in the healthy lung. (B) Corresponds to a partial left pneumothorax, with axilar symphysis; the stump shows in its lower part an opacity due to visceral pachypleuritis; absence of irrigation in the stump and very much increased circulation in the healthy lung.

visceral pachypleuritis (Figure 7a) and the last due to infiltration, visceral pachypleuritis and symphysis (Figure 7b),

d) complication with serofibrinous effusion: 2 cases (Figure 8),

e) complication with purulent effusion: 2 cases (Figure 9).

The results obtained agree almost completely with the conclusions of Celis et al.,[7] who have found in patients with pneumothorax "a decrease, without abolition, in the functional pulmonary irrigation; this decrease is related to the extent of the tuberculous process, the degree of the collapse, its age, the existence of pleural effusions, the thickening and stiffness of the visceral pleura."

Evidently the values of the pleural pressure, determining the degree of the collapse, also have a certain influence on the circulation, according to the opinion of L. and A. de Carvalho,[10,12] but we believe that among all causes acting on the circulation of the collapsed lung, the processes of infiltration or atelectasis (before or after the beginning of the treatment), and especially pleural complications (which can even abolish the functional circulation in the stump), all of them have a particular importance.

III. *Bilateral pneumothorax:* We have accomplished an angiopneumographical study in just one case, which we believe to be the first in medical literature. It may be observed in this case that the arterial and venous circulation is the same in both lungs.

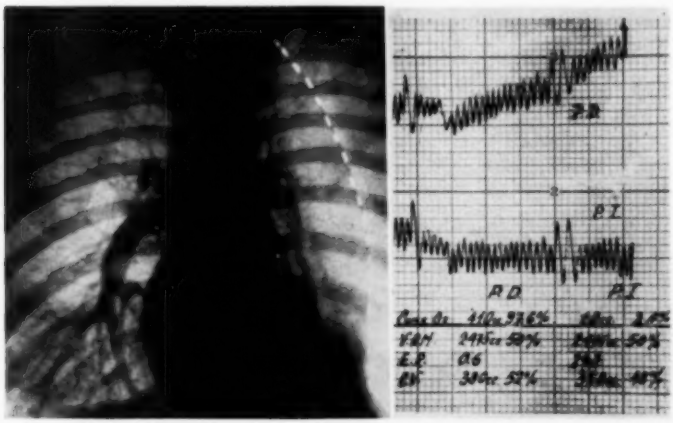

FIGURE 8: Refers to a left hydropneumothorax, with good collapse and visceral pachypleuritis; in the right lung circulation is very increased; "amputation" of the left branch of the pulmonary artery. The broncospirogram shows that while the ventilation remains almost the same in both lungs, the hematosis (oxygen consumption) takes place practically only in the right lung.

which means that the resistance opposed by both stumps to the flowing of blood is practically the same (Figure 10).

IV. *Re-expansion of the lung after pneumothorax:* Of the eight cases studied, four were pneumothorax maintained without any parenchymatous or pleural complications during periods of time varying between 24 and 40 months. The remaining four refer to pneumothorax complicated by serofibrinous fluid.

The angiopneumographies we have done show in the first four cases only a moderate reduction in the circulation of the re-

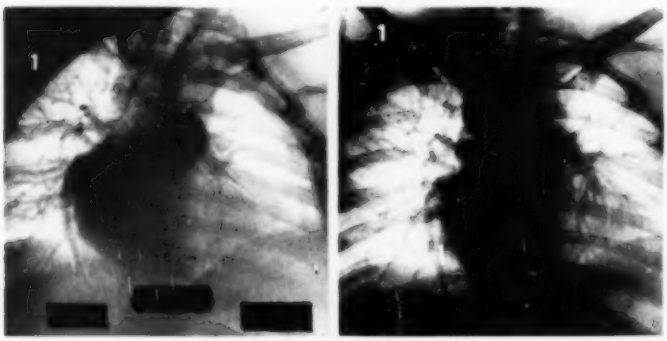

FIGURE 9: Left postpneumothorax empyemata. The left plate shows in the left lung an expansion of the pulmonary arterial branch, with few ramifications having the aspect of sluggish circulation. In the right plate, obtained one year after decortication, better irrigation in the left lung is observed, showing that its function has improved.

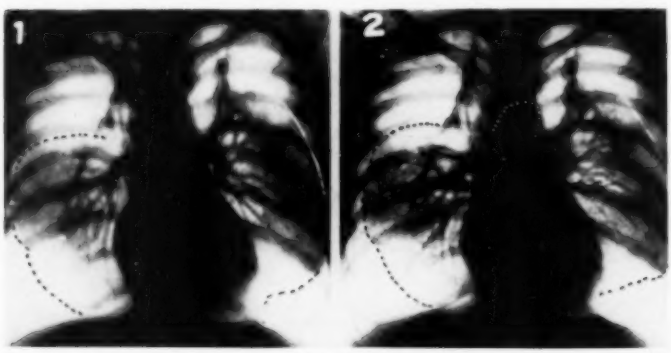

FIGURE 10: Bilateral pneumothorax, maintained in hypotension, with clear stumps with symphysis in both apices. The arterial (1) and venous (2) circulation of both stumps has the same character; the aorta appears from the second plate of the series on, showing that the circulation is accelerated.

expanded lung (Figure 11) while the remaining ones (pneumothorax with complications) show a marked reduction of irrigation, which is rendered evident by the absence of arterial branches, as well as by the appearance of a sluggish circulation (Figures 5a and 5b).

This clearly proves that the collapse (even when maintained for a relatively long period) has a small influence on the circu-

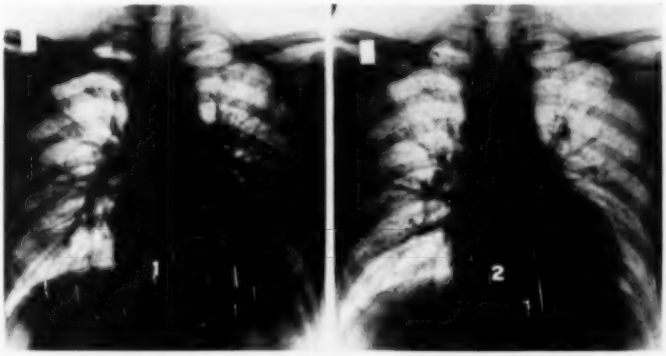

FIGURE 11: Re-expanded lung after right pneumothorax maintained in hypotension during 30 months; a section of adhesions had been performed, without complications; re-expansion of the lung two months previously. Good arterial circulation (1) is noted in the right lung; the venous branches appear in the second plate (2). The good arterial and venous circulation in the right lung show that its function is good.

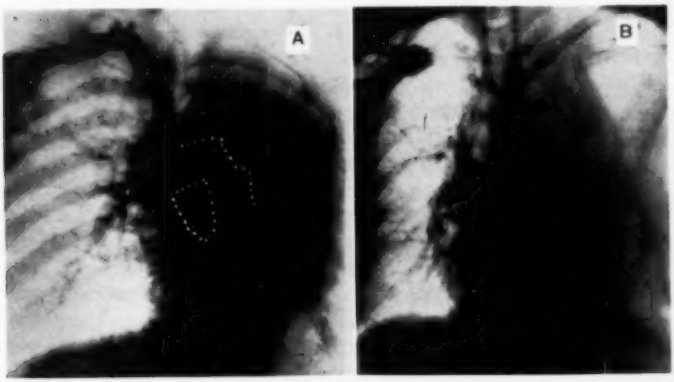

FIGURE 12: Total atelectasis. (A) Corresponds to a neoplasm of the left main bronchus. (B) Corresponds to a tuberculous lesion of the left main bronchus and thoracoplasty of nine ribs. "Amputation" of the left branch of the pulmonary artery is observed in both cases.

lation in the re-expanded lung, provided that pleural complications have not arisen. We want to point out that in three of the first group of four cases a section of the adhesions had been performed.

V. *Pachypleuritis:* Two of the six patients under observation suffered from right and four from left pachypleuritis. The beginning of the pleural process was the appearance of a serofibrinous effusion during pneumothorax in three cases; empyemata complicating the pneumothorax in one case; traumatic hemothorax in one case; and inflammatory pleural effusion, not treated, in one case. The first four patients were analyzed, when we studied the re-expansion of the lung, after complicated pneumothorax.

Not taking into consideration the factor causing the pachypleuritis, the results of these six observations are quite similar. In the affected area a great reduction of irrigation can be noticed, observing both the absence of the arterial branches and the sluggish appearance of the circulation (Figures 5a and 5b); this reduction (which is proportional to the intensity of the pachypleuritis) is much more important than could be expected through observations of ordinary plates. An increase in the irrigation may be observed in the opposite lung.

VI. *Fibrothorax:* Two cases were studied, both localized in the left lung: one started from the parenchyma and the other was the consequence of an untreated inflammatory pleural effusion.

In spite of the different origins they act in a similar way upon the circulation of the affected areas. As a matter of fact, the first case shows complete lack of irrigation in one half of the lung and sluggish circulation in the other half (Figure 4); the second case shows an "amputation" of the left branch of the pulmonary artery (Figure 3b). In both cases the circulation of the healthy lung is increased.

VII. *Partial stenosis of a main bronchus:* We have only been able to observe one case of pure bronchial stenosis, that is, without parenchymatous or pleural conditions which might, by themselves, influence the pulmonary irrigation.

In our case, the angiopneumography shows a sluggish and greatly reduced circulation in the lung with the stenosis; thus we cannot agree with the idea of a short circuit in such cases, as Vaccarezza and Soubrié[13] support in their paper.

VIII. *Complete atelectasis:* The five patients studied had atelectasis of the left lung due to different causes: two were due to neoplasm of the main bronchus; two to total thoracoplasty, performed because of a tuberculous process of the lung; and one to tuberculosis of the main bronchus and total thoracoplasty.

In spite of the variety of provoking factors, the results of all these observations are very much the same. In all the cases one

can notice a real stoppage in the flow of the opaque substance at the branch corresponding to the pulmonary artery, which appears as "amputated," without visible ramifications (Figures 12a and 12b). This stoppage is due very probably to the diffused resistance which the atelectatic lung offers to the flow of the blood, and not to an intrinsic or extrinsic arterial obstacle. In this group of cases too, the circulation of the healthy lung is increased.

IX. *Pulmonary decortication:* In two of the cases formerly analyzed, one in the group of pneumothorax complicated by empyema and the other in the group of pachypleuritis, we have been able to repeat the angiopneumographic examination after a pulmonary decortication. In both cases may be noticed a rather remarkable improvement of the irrigation, without reaching, however, the circulatory appearance of the opposite healthy lung (Figures 9a and 9b). This indicates an improvement in the pulmonary function.

Discussion

From the foregoing results, we deduce that the various processes of the lung which modify its structure, reduce in a proportional degree the irrigation of the affected parenchyma. The mechanism of this circulatory deficit has been already discussed by the authors and by Celis et al.[7]

The angiopneumographic examination is a faithful guide for the estimation of the local function of the lung in the different processes studied. We believe we have factual support to arrive at the following conclusions:

In accordance with our paper on bronchospirometry[4] and with those of Pinner et al.,[14] local pulmonary processes of the ulceroexudative type cause a reduction in the respiratory function, which is moderate and proportional to the extent of the process.

Bronchospirometries, carried out by the authors[4] and by Bjorkman[5] and by Vaccarezza and Soubrié,[15] confirm that the pulmonary collapse in itself does not much reduce the respiratory function; this moderate reduction is proportional to the degree of the collapse. Bronchial, parenchymal and especially pleural complications are the cause of a very marked diminution in function, which in certain cases may even disappear.

In the expanded lung also, the pleural processes greatly influence the circulatory and respiratory functions, whatever the cause may be, either primary processes or complications of therapeutic pneumothorax (Bjorkman,[5] Besançon et al.,[16] Pinner et al.,[14] Arnaud et al.,[17] Vaccarezza and Soubrié[18]).

The angiopneumographic examinations by Celis et al.[7] and several bronchospirometric studies already mentioned, carried out almost all of them on patients suffering from pachypleuritis, fol-

lowing abandoned pneumothorax with resorbed effusions, might suggest the idea of the functional irreversibility of pneumothorax. On the contrary, we think, as some of our cases show, that of all the collapse therapy methods, pneumothorax is the one which causes the least functional mutilation, provided a correct prescription and technique are followed in order to reduce its possible complications to a minimum.

In the cases of fibrothorax, in which the parenchymal cirrhosis is added to the pleural process, the respiratory function is practically reduced to zero.

Partial bronchial stenosis greatly reduces the function of the lung, as can be seen from our bronchospirometric study and those by Arnaud et al.[17] and Vaccarezza and Soubrié.[18]

When the bronchial stenosis produces parenchymal atelectasis, the function reduces itself to zero. The same thing happens when the atelectasis is of surgical origin.

Pulmonary decortication reestablishes in a larger or smaller, but anyway definite, degree the function of the lung.

SUMMARY AND CONCLUSIONS

A comparative angiopneumographic and bronchospirometric study was done in a group of 24 patients with definite pathological conditions of the lung, that essentially affected only one lung.

We have observed a definite relation between both methods, in the sense of a reduction of both the respiratory and circulatory functions of the abnormal lung. The following interpretation is offered: the pathological condition induces parallel changes on the circulatory and respiratory function at the same time. The phenomenon of circulatory shunt in lung pathology becomes less important than it was formerly though.

It is probable that the angiopneumographic study will take the place of the bronchospirometric study at least in the majority of cases. In practice the first named study makes more complete the information obtained by the latter; it also presents the additional advantages of making possible an appreciation of the function of the different segments of each lung.

We have also done 41 angiopneumographies on 37 patients suffering from different pathological processes of the lung, almost all of them of tuberculous origin. Based on our results we arrive at the following conclusions:

1) In ulcero-exudative tuberculosis there exists a diminution of the respiratory function, which is moderate and proportional to the extent of the process.

2) In unilateral pneumothorax, maintained by hypotension, with a clear and elastic stump, one can notice a certain diminution of

the function; on the contrary the function is very much reduced or abolished in cases complicated by atelectasis of the stump or by serofibrinous or purulent pleural effusion.

3) Logically, when initial parenchymatous conditions are equal, the residual capacity of a lung, after the pneumothorax has been abandoned, is inversely proportional to the degree of the complications which might arise.

4) In pachypleuritis and in partial stenosis of a main bronchus, the respiratory function is very much reduced, much more so than could be expected through observation of ordinary plates.

5) The respiratory function disappears in fibrothorax and in cases of atelectasis.

6) Pulmonary decortication, carried out because of previous pachypleuritis, causes an improvement in the respiratory function, demonstrated by the improvement of the pulmonary circulation.

RESUMEN Y CONCLUSIONES

Se ha hecho el estudio comparado angioneumográfico y broncoespirométrico en una serie de 24 enfermos con intensos procesos patológicos que afectan predominantemente un solo pulmón.

Se ha observado una clara correlación entre ambos métodos, en el sentido de una reducción de las funciones respiratoria y circulatoria en el lado enfermo.

Se deduce que los procesos patológicos estudiados alteran al mismo tiempo las dos funciones, lo cual tiende a restar importancia al fenómeno del corto circuito en patología pulmonar.

Es muy probable que el examen angioneumográfico pueda sustituir al examen broncoespirométrico en casi todos los casos; prácticamente, lo complementa siempre y además tiene la ventaja de permitir apreciar la función en los diferentes segmentos de cada pulmón.

También, se han realizado 41 angioneumografías en 37 pacientes afectados de diversos estados patológicos del pulmón, casi todos de origen tuberculoso. Sobre la base de lo anteriormente dicho, los resultados obtenidos nos autorizan para emitir las siguientes conclusiones:

1) En la tuberculosis úlcero-exudativa existe una disminución de la función respiratoria, que es moderada y proporcional a la extensión del proceso.

2) En el neumotórax unilateral, mantenido en hipotensión, con muñón claro y elástico, se aprecia una discreta disminución de la función; por el contrario, ella está muy disminuída o abolida en los casos complicados con atelectasia del muñón o con derrames serofibrinosos o purulentos.

3) Lógicamente, a igualdad de condiciones parenquimatosas ini-

ciales, la capacidad residual de un pulmón, después de abandonado el neumotórax, es inversamente proporcional a las complicaciones ocurridas durante su realización.

4) En la paquipleuritis y en la estenosis parcial de un bronquio fuente, la función respiratoria está muy disminuída, mucho más de lo que podría hacer suponer el examen de la radiografía simple.

5) La función respiratoria está abolida en el fibrotórax y en la atelectasia.

6) La decorticación pulmonar, realizada por paquipleuritis, determina una mejoría de la función respiratoria, demonstrada por una mejoría de la circulación pulmonar.

RESUME ET CONCLUSIONS

Les auteurs ont réalisé une comparaison de l'angiopneumographie et de la broncho-spirométrie chez 24 malades, atteints d'affections définies, localisées électivement au poumon.

Ils ont observé une relation très nette entre les deux méthodes, avec réduction dans les deux cas de la fonction respiratoire et de la fonction circulatoire du poumon anormal. Ils l'interprètent comme étant la preuve que les altérations pulmonaires provoquent une modification parallèle des fonctions circulatoire et respiratoire. Le phénomène du "court-circuit circulatoire" en pathologie respiratoire parait beaucoup moins important qu'on ne le pensait autrefois.

Il est probable que l'étude angiopneumographique prendra la place de la broncho-spirométrie dans la majorité des cas. En pratique, la première de ces méthodes complète les informations qui peuvent être obtenues par la seconde. Il s'y ajoute l'avantage de rendre possible l'appréciation de la fonction des différents segments de chaque poumon.

Les auteurs ont également pratiqué 41 angiopneumographies chez 37 malades, atteints d'affections variées du poumon, dont la plupart étaient d'origine tuberculeuse. Leurs résultats les ont amené aux conclusions suivantes:

1) Dans la tuberculose ulcéro-caséeuse, il y a une diminution de la fonction respiratoire qui reste modérée et proportionnée à l'extension des lésions.

2) Dans le pneumothorax unilatéral, maintenu en hypotension, avec un parenchyme clair, ayant gardé toute son élasticité, on peut noter une certaine diminution de la fonction. Mais par contre, la fonction est très réduite ou même abolie dans les cas qui sont compliqués d'atélectasie pulmonaire ou d'épanchement pleural, soit séro-fibrineux, soit purulent.

3) Logiquement, les conditions parenchymateuses étant égales, la capacité résiduelle du poumon après abandon du pneumothorax

est inversement proportionnelle au degré des complications qui ont pu survenir.

4) Dans les cas de pachypleurite et dans les stenoses partielles de la bronche souche, la fonction respiratoire est très réduite, beaucoup plus encore que l'on aurait pu l'imaginer.

5) La fonction respiratoire est nulle dans le fibrothorax et dans les cas d'atélectasie.

6) La décortication pulmonaire entreprise pour lutter contre la pachypleurite réalise une amélioration de la circulation pulmonaire que démontre l'amélioration de la fonction respiratoire.

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The Management of Esophageal Perforations

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The successful handling of esophageal perforations has changed considerably during the past decade. Prior to 1940, esophageal perforation, regardless of the etiology involved, carried with it a fearful morbidity and unless surgical drainage was immediately instituted, a dependable mortality. In the recent literature, however, there have appeared several articles setting forth a newer concept regarding the management of known esophageal disruption with a sizable reduction in both morbidity and mortality statistics.[1,2,3,5] The recent and rapid strides in thoracic surgery greatly aided by the coincidental discovery and production of versatile and germ destroying antibiotics has been responsible in a large measure for the altered approach to this catastrophe.

During the past four years 16 cases of esophageal perforation have been seen by us (D.J.D. and Paul C. Samson). The etiology concerned has varied widely and the treatment depended greatly on many factors which will be individually considered.

Case Reports

Case 1: A.G., aged 52, was admitted to the hospital because of an impacted food bolus within the lower esophagus. Esophagoscopy was performed under general anesthesia on June 4, 1949 without difficulty. During extraction of the bolus the patient's relaxation was inhibited by lightening of the anesthetic and there was considerable gagging. Perforation was not suspected and the endoscopic procedure required 25 minutes. Fourteen hours following, his temperature rose to 101 degrees F. and he complained of acute tenderness in the left cervical area. Palpation of the neck revealed tenderness and a small area of crepitus directly inferior to the left mastoid. Lipiodol swallow and a heavy film revealed mediastinal emphysema with suspended lipiodol in the cervical area. He was taken to surgery 25 hours following esophagoscopy where a linear tear in the posterior esophagus directly over the sixth cervical vertebra was repaired through a left cervical approach. Recovery was uneventful and he was discharged taking a regular diet seven days later. Intensive penicillin therapy was administered during his hospital stay.

Case 2: M.K., aged 29, a young girl circus performer entered the hospital on May 15, 1950 for diagnostic esophagoscopy in investigation of an unexplained dysphagia. The procedure was performed under general anesthesia and without difficulty. Extrinsic pressure, later proved to be caused by caseous tuberculous lymph nodes, was noted in the mid esophagus and the entire examination required approximately 40 minutes. Perforation was not suspected; however, immediately on awakening the patient complained of undue soreness in the cervical area and within 12

hours her temperature rose to 101 degrees F. There was point tenderness in the mid portion of the left sternomastoid muscle and she held her neck rigidly. High perforation was suspected and lipiodol swallow and comparative lateral cervical films confirmed this suspicion (Figures 1 and 2). Left anterior cervical mediastinotomy was performed on May 17, 1951, 41 hours following the perforation and a linear tear in the posterior wall of the esophagus directly over the sixth cervical vertebra was repaired over an indwelling Levine tube. Massive doses of penicillin, 600,000 units two times daily, were administered and the tube was removed within three days at which time liquid diet was started. She was discharged six days following esophagoscopy and was readmitted three weeks later when via right thoracotomy the lymph nodes were removed as well as an old abscess drained. She has since returned to her aerial occupation.

Case 3: G.S., aged 46, was admitted to the hospital for pre-operative investigation of an esophageal diverticulum. Esophagoscopy was performed on February 2, 1951, under general anesthesia and was carried out without incident. The time required for the procedure was 18 minutes. Twenty-four hours later he complained of pain on swallowing and slight tenderness in the left cervical area. Temperature was 100 degrees F. and there was slight leucocytosis (9500). Penicillin, intravenous therapy and nothing by mouth for 24 hours did not improve the situation. Tenderness in the neck was well localized over the mid portion of the left sternomastoid muscle where there was definite redness of the skin. The white cell count rose to 16,600 and cervical x-ray films showed an increase in mediastinal emphysema. Forty-eight hours following the esophagoscopy he was taken to surgery where anterior left cervical mediastinotomy was

FIGURE 1

FIGURE 2

Figure 1, Case 2: Pre-esophagoscopy lateral cervical roentgenogram showing normal distance between anterior border of vertebral bodies and trachea.—*Figure 2, Case 2:* Post-esophagoscopy roentgenogram demonstrating widening of distance between anterior border of vertebral bodies and trachea with lipiodol at site of perforation.

performed. At the level of the seventh cervical vertebra between the posterior wall of the esophagus and the vertebra purulent foul-smelling material was encountered. No attempt was made at closure of the observed perforation. A tissue drain was inserted and the wound loosely closed. Mouth feedings were withheld for five days during which time penicillin and intravenous therapy were continued. The drain was removed on the third postoperative day and the patient was discharged 10 days after the drainage procedure, entirely asymptomatic.

Case 4: J.S., aged 61, was admitted to the hospital for investigation of a lower esophageal obstruction presumably due to a carcinoma. Esophagoscopy was performed under curare and pentathol anesthesia. Biopsy of a tumor at the cardiac end of the esophagus revealed adenocarcinoma and two hours following this 30 minute procedure bilateral cervical emphysema was present. Antibiotics in large doses were given, parenteral feedings instituted and his condition appeared to improve. However, four days later he became toxic, emphysema rapidly increased and 96 hours following perforation a foul-smelling abscess between the cervical vertebrae and the esophagus was drained through a left cervical mediastinotomy. His downward course continued and he expired 12 hours later.

Case 5: W.B., aged 40, choked while eating a pork chop 24 hours prior to our consultation. He felt a small piece of the bone lodge in his throat and consulted his family physician. With the patient in the sitting position an attempt was made to blindly pass a curved probe into the upper esophagus and this was immediately followed by a moderate hemorrhage. On admission to our service his temperature was 101 degrees F. and he complained of soreness in the throat. On April 22, 1947 under pentathol anesthesia esophagoscopy was performed and a red edematous esophageal orifice was seen. Immediately below the cricopharyngeal level

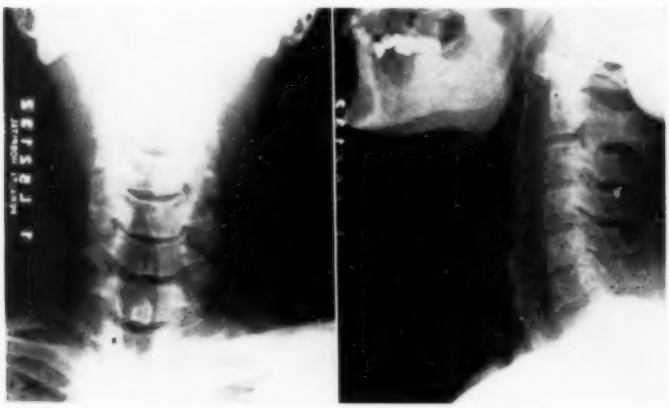

FIGURE 3a FIGURE 3b

Figures 3a and 3b, Case 5: A.P. and lateral cervical roentgenograms showing bilateral upper mediastinal emphysema following instrumental removal of bone fragments from upper esophagus. Trapped air in retropharyngeal space is best demonstrated on lateral projection.

several small bone particles were seen and extracted. The procedure required 27 minutes. Within 10 hours it was noted that the neck was visibly swollen, crepitus could be palpated along either sternomastoid muscle and the temperature was 101 degrees F. An x-ray film taken at this time showed evidence of cervical emphysema (Figure 3) and he was given 100,000 units of penicillin every three hours, as well as intravenous fluids and saline throat irrigations. This routine was followed for five days at which time the symptoms subsided and on April 30, 1947 he was discharged without complaint and was on a regulation diet.

Case 6: D.M., choked on a small chicken bone four days prior to admission to the hospital. He was seen shortly thereafter by his family physician and a stomach tube was passed in an attempt to dislodge the foreign body which was felt to be in the upper esophagus. The patient continued to notice dysphagia and there was moderate pointed pain in the left cervical area but no palpable emphysema. These symptoms continued and on admission on August 23, 1947 he had a temperature of 100.8 degrees F. Esophagoscopy shortly following admission showed an edematous esophageal opening with gross evidence of mucosal trauma and immediately at the level of the cricopharyngeal region a small chicken done was observed. The foreign body was located in a transverse position directly across the esophageal lumen necessitating transection before removal in two separate pieces. The procedure required 45 minutes operating time and the patient ran a stormy postoperative course, the temperature reaching 104.6 degrees F. five hours later. Every three hours, 100,000 units of penicillin were given, intravenous fluids were administered, but nothing by mouth was ordered. Barium swallow taken four days later showed a pool of the opaque dyes outside of the esophageal lumen obviously at the previous site of the chicken bone (Figure 4). The temperature subsided to normal six days following esophagoscopy and

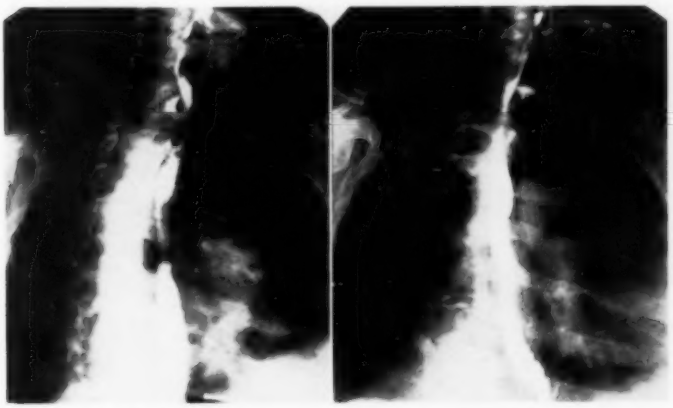

FIGURE 4a FIGURE 4b

Figure 4a and 4b, Case 6: Oblique chest roentgenograms taken three days following esophagoscopic removal of transversely impacted chicken bone. Note pooling of barium at site of esophageal perforation.

the patient remained asymptomatic. He was esophagoscoped one month later when the entire esophagus appeared normal and there was no evidence of perforation either by direct inspection or pooling of swallowed barium.

Case 7: C.M., aged 71, was esophagoscoped in investigation of a lower esophageal lesion which proved to be of a granulomatous nature. The procedure performed under local anesthesia on April 5, 1947 was done with some difficulty and as the instrument was advanced the patient turned himself on the table in an effort to remove the esophagoscope. A definite mid-esophageal perforation was at once recognized because of the appearance of the right lung through the lumen of the examining instrument. A Levine tube was immediately inserted into the stomach, penicillin therapy instituted and an x-ray film taken the same day showed a 25 per cent right pneumothorax confirming the operator's impression of pleural entry. Liquid diet was started 72 hours later and he made an uneventful recovery.

Case 8: S.D., aged 46, was esophagoscoped two days following the swallowing of a fragment of pork chop bone. He was admitted to the hospital on March 15, 1946 because of inability to swallow and under general anesthesia 10-15 grams of undigested meat with bone fragments were removed from the lower esophagus. The operative procedure required 55 minutes and there was gross evidence of maceration of the lower esophagus but no obvious perforation. On the following day, 18 hours after esophagoscopy the temperature rose to 102 degrees F. There were 24,800 white blood cells and cervical subcutaneous emphysema was palpable. X-ray films verified the emphysema and showed evidence of pneumonitis in the right lung field. Every three hours 50,000 units of penicillin were given. Intravenous feedings were administered and all diet was

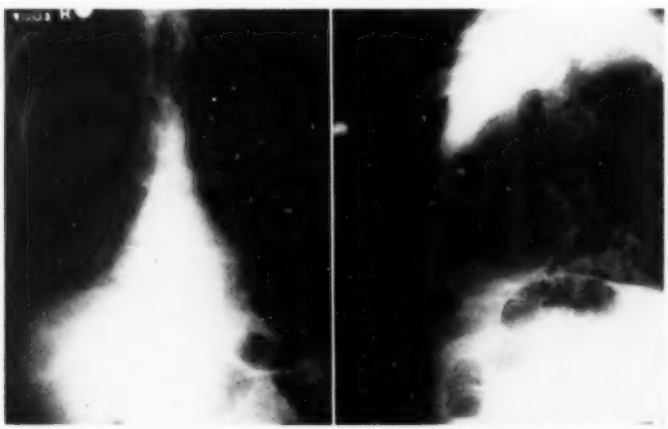

FIGURE 5a FIGURE 5b

Figure 5a and 5b, Case 10: A.P. and lateral chest roentgenograms showing inferior mediastinal abscess with fluid level caused by visual dilatation of lower esophageal stricture.

discontinued. The temperature subsided within three days, liquids were then started by mouth and he was discharged six days later on a regular diet and was asymptomatic.

Case 9: E.G., aged 66, a diabetic female was admitted to the hospital because of progressively increasing dysphagia. Barium studies showed a stenosis of the lower esophagus and on December 8, 1947 esophagoscopy was performed. A fibrotic stenosis was observed and dilatation performed. Perforation was suspected and the procedure required 25 minutes. She was placed on heavy doses of penicillin and supportive therapy, but continued to run a septic course. Three weeks later a rib resection drainage of a left empyema was performed. Within a week her swallowing improved and she was discharged from the hospital on January 18, 1948 with empyema drainage still present. She continued to drain purulent material and finally succumbed three months later presumably of chronic suppuration.

Case 10: J.J., aged 72, has been under the care of a competent endoscopist for 20 years during which time frequent esophageal dilatations had been performed for an esophageal stricture of unknown etiology. In that interval he had been dilated about 35 times without incident. He was first seen by us on June 13, 1950, five days following a routine dilatation, with chest pain, temperature of 102 degrees F. and considerable epigastric discomfort. An x-ray film taken June 13, 1950 revealed a mediastinal fluid collection (Figure 5). A right posterior extrapleural mediastinotomy with resection of the ninth and 10th ribs was performed on June 14, 1950 and a putrid abscess was drained. Three weeks later a right empyema was likewise drained. He gradually fully recovered and complete healing occurred within a three month period. Penicillin therapy was administered during his hospital stay of six weeks.

Case 11: A.R., aged 50, was first seen by us on July 2, 1948 when she was admitted to the hospital via ambulance. According to history she

FIGURE 6 FIGURE 7

Figure 6, Case 11: Chest roentgenogram taken 21 days following endoscopic perforation of lower esophagus demonstrating complete collapse of right lung with pyopneumothorax.—*Figure 7, Case 11:* Film taken 12 days following right pulmonary decortication with pressure closure of esophago-pleural endoscopic perforation.

had been esophagoscoped for cardiospasm on June 14, 1948. Signs of lower esophageal perforation became manifest 12 hours later. Large doses of penicillin and streptomycin were administered, mouth feedings were withheld and rib resection drainage of a right empyema was performed four days following perforation. The drainage tube was removed two days prior to this admission when a phlegmon of the right posterior chest wall was present. X-ray film on this admission showed evidence of fluid which proved to be empyema with almost total collapse of the right lung. Any attempt at swallowing resulted in the immediate appearance of the swallowed material on the chest dressing. A Levine tube was inserted and she was maintained entirely on intravenous feedings. Penicillin was given in large quantities and on July 5, 1948 suction drainage of the empyema succeeded in removing all of the fluid but the underlying lung failed to expand (Figure 6). Any attempts at swallowing food again resulted in its appearance in the chest drainage bottle. On July 15, 1948 right thoracotomy was performed, the right lung was completely decorticated and no actual esophageal perforation could be demonstrated. The lung expanded readily and brought about pressure sealing of the esophageal opening (Figure 7). Five days later the Levine tube was removed. She was started on a liquid diet and in two weeks was discharged fully recovered. The final x-ray film taken on July 26, 1948 showed complete re-expansion of the lung.

Case 12: H.D., aged 55, experienced severe epigastric pain immediately following an emesis of large amounts of food and alcoholic beverages. This episode occurred during the early morning hours and he was immediately seen by a physician. He was in shock, and the severe mid-epigastric pain was not influenced by one-half grain of morphine. He was admitted to the hospital where x-ray investigation of the esophagus with lipiodol swallow justified the diagnosis of lower postemetic esophageal perforation. His condition rapidly deteriorated even during the time required for x-ray study. The pain increased in severity and he developed the nasal tone of voice so typical of mediastinal pressure. The blood pressure dropped to 80/40. Following administration of 600 cc. of plasma a left thoracotomy was performed. On opening the left side of the chest a sympathetic pleural effusion of approximately 500 cc. was encountered. Displacement of the lung uncovered a blackened mediastinal pleura from the diaphragm to the aortic arch. The pleura was incised and a two and one-half inch esophageal perforation running in a longitudinal direction one inch above the diaphragm was seen. The esophagus was closed directly with fine silk interrupted sutures and the chest was closed after water seal drainage of the pleura. A Levine tube was left in place for three days and the chest drainage tube was removed on the third postoperative day. He was discharged without complaint on January 3, 1949, 15 days following thoracotomy.

Case 13: H.K., aged 42, had always complained of a "weak stomach" and claimed that he vomited very easily. On June 2, 1949 closely after imbibing a large quantity of alcoholic beverage and food he had an unusually severe attack of vomiting followed at once by an emesis of about one-half cupful of blood and severe mid epigastric and lower chest pain. He was immediately seen by his family physician and the chest pain and prostration were of such an extent that he was immediately hospitalized. Chest x-ray films showed evidence of left pleural effusion.

air and fluid in the mediastinum and emphysema of the soft tissues of the neck. A diagnosis of ruptured esophagus was made on the basis of the plain x-ray film, and lipiodol swallow showing the opaque material free in the mediastinum confirmed this impression. He showed evidence of mild shock. His temperature was 97 degrees F., and the white cell count was 17,950. There were definite rales at the left lung base and palpable emphysema in the neck. Seven hours following the onset of symptoms left thoracotomy was performed. On opening the chest, stomach contents were free in the pleural cavity and there was a ragged two inch longitudinal tear in the esophagus just above the diaphragm. With each respiratory movement of the diaphragm, stomach content was regurgitated through the esophageal rupture. A suction tip was passed into the stomach via the esophageal rupture and much of the partially digested material was removed. The pleural cavity was thoroughly irrigated with saline solution, the esophageal rent was closed with interrupted fine silk sutures, the pleura was drained and the chest closed. Recovery was complicated only by severe penicillin dermatitis, and he was discharged from the hospital 14 days later on a regular diet and without complaints.

Case 14: G.B., a 68 year old female choked on a large chicken bone on March 11, 1951. She called her regular physician who administered a sedative hypodermically. She did not obtain relief to any degree and on March 14, 1951 became worse with fever and epigastric pain. She was admitted to the hospital and barium swallow demonstrated a foreign body in the lower part of the esophagus which had perforated the esophageal wall (Figure 8). Esophagoscopy was immediately performed and at the cardiac end of the esophagus an edematous, traumatized mucosa was

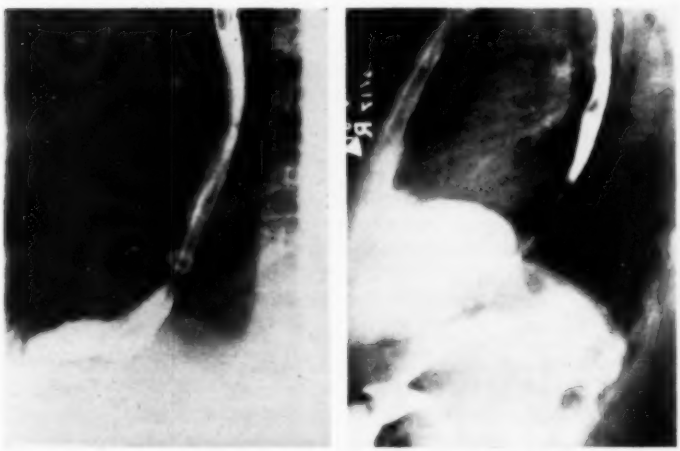

FIGURE 8a FIGURE 8b

Figure 8, Case 14: (a) Barium-filled esophagus showing chicken bone penetrating esophageal wall above diaphragm.—(b) Esophragram taken two weeks following removal of chicken bone.

seen. The large chicken bone, two and one-half inches in length, was grasped and maneuvered free of its attachments to the esophageal wall. Mouth feedings were discontinued, penicillin, aureomycin and intravenous therapy were administered and she made an uneventful recovery being discharged on a full diet six days later.

Case 15: E.W., aged 52, was first seen 14 hours following abdominal repair of a hiatal hernia. She was in extreme shock, was dyspnoeic and there were absent breath sounds over the entire left chest. Needle aspiration of the left pleural cavity disclosed what appeared to be stomach content and closed intercostal drainage brought about immediate clinical improvement. A large esophageal perforation was demonstrated by the immediate appearance of ingested food in the chest drainage bottle. A Levine tube was inserted, Wangensteen suction instituted, intravenous fluids and heavy doses of penicillin were given. X-ray films showed evidence of hydropneumothorax on the left side with 50 per cent collapse of the lung. On September 30, 1948, 14 days following the insertion of the intercostal tube left thoracotomy disclosed a collapsed left lung covered with a heavy exudative peel and a two and one-half inch perforation in the esophagus just above the diaphragm. The esophagus was closed with several interrupted catgut sutures, the lung was decorticated and suction drainage of the pleural cavity established. Wangensteen suction of the stomach was carried out postoperatively; however, evidence of continued esophageal leak prompted a gastrostomy on October 18, 1948. The gastrostomy was allowed to function until December 1, 1948 when all chest drainage had ceased and she was returned to a regular diet. No further surgery was required and final check-up one year later was entirely satisfactory.

Case 16: M.L., aged 58, presented himself with history of cardiospasm of one year's duration. This diagnosis was confirmed by x-ray studies and esophagoscopy was entirely within normal limits. The symptoms persisted in spite of medical therapy and in view of this man's progressive weight loss, dilatations were felt in order. Under local anesthesia and with fluoroscopic guidance a Plummer-Vinson dilator bag was inserted and moderate pressure was exerted with the bag at the esophagogastric junction. He did not complain until four or five hours later, when he reported mild epigastric discomfort. The following day the pain became more severe, temperature was elevated to 100 degrees F. and barium swallow showed a rupture of the lower esophagus with barium in the peritoneal cavity. Laparotomy was performed on February 15, 1950, 36 hours following dilatation and a small tear at the esophagogastric junction was repaired. His recovery was complicated by a subphrenic abscess which was subsequently drained.

Discussion

Of the 16 cases of esophageal perforation presented in this series, 11 can be attributed to direct trauma caused by an endoscopic procedure. Because of the importance of prompt recognition and adequate treatment of instrumental esophageal rupture, particular attention shall be given to the 11 such cases in this series, six of whom had cervical perforations and the remaining five evidence of lower esophageal penetration.

Endoscopic Perforations of Cervical Esophagus:

In the consideration of the six cases of cervical perforation it is of remarkable interest to note that four cases were esophagoscoped because of investigative procedures involving the lower one-third of the esophagus, while the remaining two cases had definite penetrating foreign bodies in the cricopharyngeal region. The technical procedure performed in each of the six cases was carried out with ease insofar as the introduction of the instrument was concerned so that direct penetration of the esophageal wall with the tip of the esophagoscope was not considered likely. A careful review of the operative report in the four investigative esophagoscopies shows that the total time consumed during each procedure averaged well over 35 minutes. All four perforations occurred directly over the region of the sixth and seventh cervical vertebrae and each showed a linear tear approximately one and one-half cm. in length. It would, therefore, seem reasonable to assume that perforation in these four cases was brought about by prolonged pressure of the body of the esophagoscope resting on the prominent surfaces of the sixth and seventh cervical vertebrae. Each of the four cases were surgically treated by cervical mediastinotomy. In two, the esophageal tear was closed primarily and the third responded to simple drainage while the fourth case of this group was drained after 96 hours and succumbed shortly thereafter.

From these results it seems logical to assume that all instrumental cervical perforations of the esophagus should be treated by primary cervical mediastinotomy and closure of the rent as soon as the diagnosis can be made. This is reasonable from our results as the fatality in our group resulted from too long an interval between recognized perforation and corrective surgery. In these cases a matter of hours can be the difference between primary closure, drainage and failure. In case 1 surgical repair was accomplished in a clean field 25 hours following cervical esophageal rupture. In case 2, mediastinotomy was performed 41 hours following endoscopic perforation and closure was done in an already "musty" field. In case 3 performed 48 hours after rupture, frank purulent material was encountered making direct closure undesirable and hospitalization prolonged, while case 4 drained 96 hours following rupture proved to be too late for salvage.

In the other two cases of penetrating foreign bodies in the upper esophagus (Cases 5 and 6) it is admittedly possible that the introduction of the scope may have caused further penetration of the already embedded bony spicules. In both cases the fact of mediastinal invasion was definitely proved by x-ray and clinical signs, still supportive measures and antibiotic therapy were most effec-

tive without surgical intervention. Pressure of the esophagoscope on the already embedded bone spicules before removal was accomplished brought about a puncture mediastinal wound rather than a gross linear tear. It is probably because of the mediastinal pin point opening and lack of gross contamination plus antibiotic support that fatal sepsis did not occur.

Endoscopic Perforations of Lower Esophagus:

Of the five instrumental lower esophageal disruptions, two (Cases 7 and 8) healed with symptomatic and supportive treatment, the third (Case 9) required drainage of a left empyema and finally succumbed as a result of chronic suppuration and the remaining two cases (Cases 10 and 11) recovered following late repairative surgical procedures.

The two symptomatically treated cases were similar in the respect that retching and gagging were prominent reactions in both during the distal advancement of the esophagoscope. Case 7 was a diagnostic procedure for a lower esophageal lesion, which was performed under local anesthesia. The patient rolled himself on the table during the advancement of the instrument, and the immediate suspicion of lower perforation was confirmed by x-ray demonstration of right pneumothorax.

Case 8 was esophagoscoped because of a food bolus in the lower esophagus. The procedure was done with difficulty because of straining and retching during anesthesia and mediastinal penetration was probably caused by undue pressure with the tip of the instrument on an already macerated esophageal mucosa. The explanation of the probable etiology in these patients is much easier than the reasons for their recovery. These individuals were seen early in this series and fortunately responded to heroic conservatism.

The third case in this group (Case 9), a severe diabetic, was examined endoscopically for a fibrosing stricture of the lower esophagus. The stricture was dilated, and perforation of the lower one-third of the esophagus was suspected. Treatment was not instituted until three weeks later when a left empyema was drained and her general condition particularly with respect to diabetes made further corrective surgical therapy inadvisable.

The remaining two cases (Cases 10 and 11) of this lower instrumental perforation group represent dire situations resulting from delayed treatment. Case 10 demonstrates the ever present danger in repeated dilatations of chronic strictures even under direct vision. This elderly male had many previous dilatations of an old stricture of unknown etiology. A mediastinal abscess was drained six days following visual endoscopic dilatations. Eventual

recovery followed the subsequent drainage of an associated right empyema. Case 11 represents instrumental perforation in a relatively young individual with a normal esophagus. This 50 year old female was esophagoscoped for cardiospasm and developed immediate signs of lower perforation with right pleural involvement. She was seen by us three weeks following the incident with an esophageal pleural cutaneous fistula present in addition to an accompanying right empyema and collapsed lung. Complete recovery followed primary drainage of the right empyema, right thoracotomy and pressure closure of the fistula by re-expansion of the decorticated right lung.

In retrospect with these five cases in mind, judgment in the control of the first four seemed sound in consideration of the results obtained. The symptomatic therapy in the first two was most productive although I am sure that in light of our present concept of this complication, if similar cases of lower esophageal instrumental perforation were seen at this time thoracotomy with primary closure would be carried out. The elderly diabetic patient who was dilated and eventually had left empyema would undoubtedly not have withstood operative intervention of any kind. As regards Case 10, because of the extreme difficulty and likely impossibility of identifying the perforation in the scarred esophagus careful waiting for the development of the abscess in this 72 year old man was probably wise. In contradistinction, however, it would appear more reasonable in Case 11 where perforation resulted from an examination of a normal esophagus for cardiospasm in a relatively young individual, to institute primary closure at once before the complications of empyema, collapsed lung and fistula developed.

Non-Endoscopic Perforations of Lower Esophagus:

There were five cases in our series of non-endoscopic perforations and all seem worthy of mention both from an etiologic and therapeutic standpoint. Two cases of postemetic spontaneous rupture of the lower esophagus have been reported elsewhere by my associate, Dr. Paul C. Samson[6] and both had uneventful courses following prompt and early left thoracotomy with closure (Cases 12 and 13). A recent one (Case 14) with a penetrating foreign body in the lower esophagus responded nicely following endoscopic removal, antibiotics and administration of parenteral fluids for three days. The fourth in this group (Case 15) whose perforation was caused during the abdominal repair of a hiatal hernia recovered after a complicated and stormy course including drainage, left pulmonary decortication, late closure of the esophageal tear and interval gastrostomy. The final case of lower esophageal

rupture (Case 16) resulted from dilatation with a Plummer-Vinson bag and recovered also after a stormy course requiring closure of the opening via the abdomen and secondary drainage of a subphrenic abscess. In this latter case barium was mistakenly used as a contrast medium in the suspected esophageal perforation. In such cases where a complication of this nature is suspected, less irritating lipiodol is much to be preferred for x-ray studies.

Conclusions

Endoscopic removal of sharp bone spicules at the cricopharyngeal level may bring about pin point mediastinal penetrations because of pressure of the tip of the esophagoscope before the particles are removed. Such "stab" wounds of the mediastinum may be treated symptomatically with relative safety providing progressive clinical improvement is observed.

Prolonged operative time consumed in endoscopic procedures involving the lower esophagus may cause tears in the cervical area because of pressure of the body of the instrument over the prominent cervical vertebrae. These linear tears of the cervical esophagus should be repaired surgically as soon as the diagnosis is made.

Lower esophageal perforations due to instrumentation should be treated by thoracotomy and primary closure unless extreme debility or sclerosing luminar lesions make the surgical approach impractical.[4] Postemetic or so-called spontaneous rupture of the esophagus while a relatively rare lesion, can be diagnosed both by clinical and radiological signs and early thoracotomy with primary esophagus closure is the most effective treatment.

A non-irritating contrast medium should be used for esophageal x-ray visualization when perforation is suspected.

SUMMARY

A series of 16 cases of esophageal perforations treated in the past four years is presented. Eleven of this group had perforations directly due to endoscopic procedures, while the remaining five cases were precipitated by other causes.

The treatment of each case is outlined, a discussion of the probable etiology is given and recommendations are made for future handling of similar cases.

RESUMEN

Se presenta una serie de 16 casos de perforación del esófago, tratadas en los últimos cuatro años. Once de este grupo tenían perforaciones debidas directamente a procedimientos endoscópicos, mientras que los cinco casos restantes eran debidos a otras causas.

El tratamiento que en cada caso es descrito, discute la probable etiologia, y se hacen recomendaciones para el manejo de casos similares.

RESUME

L'auteur rapporte seize observations de perforations ossophagiennes traitées dans les quatre dernières années. Onze de ces cas avaient pour cause des manoeuvres endoscopiques, d'autres étiologies devaient être invoquées dans les cinq derniers cas.

L'auteur détermine le traitement de chaque cas, envisage l'étiologie probable et établit quelques règles pour la conduite à tenir dans d'éventuelles observations similaires.

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The Management of Some Difficulties in Pulmonary Resection*

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The innumerable difficulties and complications of pulmonary resections deserve a great deal of discussion much beyond the scope and the time allotted to this presentation.

It is our purpose to discuss in a brief manner only certain of these difficulties and to show how we try to solve the problems in some particular cases.

The three difficulties we are dealing with today are: the management of the empty space after pneumonectomy, the approach to the problem of the "short stump" and the post-resectional bilateralization.

The Empty Space After Pneumonectomy

From the beginning of pulmonary resections, chest surgeons were preoccupied by the possibilities of the empty space after excision. Several complications were foreseen: the damaging results of mediastinal displacement, with interference with the circulatory transit in the large vessels, particularly in the veins on the right side; the influence of the increasing negative pressure on the right heart and the pleural serosa; the possibility of developing effusion and eventual infection and also the influence of the displacement on the other lung.

Many procedures were planned to overcome the several difficulties and we have in the literature a number of suggestions such as the use of beef broth to elicit the formation of fibrous tissue, as advocated in the early experience of resection to the recent trend to use some foreign bodies to occupy the space.

Post-resectional thoracoplasty would be a logical solution of the problem and as a matter of fact is the most favored procedure today. However the results expected from this time honored operation to close the space are not always satisfactory.

Unless thoracoplasty is done in a radical way the space only decreases and the problem created by the resection is only less pronounced but not completely solved. It is a fact already reported that the possibility of developing cor pulmonale is not much preventable by this means. Furthermore, thoracoplasty whether done

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at the same time as the resection or afterwards means an additional risk to the patient. Also the deformity after a thoracoplasty makes the procedure rather objectionable.

As regards the prosthetic procedures consisting in the use of foreign material some disadvantages have been presented such as the poor tolerance for most of them and the possible damaging action on the mediastinal structures.

The consequence of the expansion of the other lung with extensive displacement of the mediastinal structures is not always very important however.

The lung on the other side if not diseased is able to expand under an hypertrophic process and can fill anatomically and functionally as well the space left by the excised lung.

But this is not the rule and in most cases the problem subsists.

As an example of the surprising tolerance to the displacement of the mediastinum and the favorable result of the lung hypertrophy we are describing the following:

A man (I.V.) of 40 years in whom diagnosis of lung carcinoma of the right lower lobe was made, underwent total pneumonectomy in November 1946. After an uneventful recovery the left lung expanded, displaced the mediastinum to the right side and completely filled the space of the left side.

Four and a half years after the operation and after four years of resuming his occupation as railroad conductor, he is able to run after the train for two hundred meters without dispnoea, can swim in a river of strong current for half an hour and is able to dive and swim under the surface for as far as twenty meters (Figures 1, 2 and 3).

It is an optimal case and we must readily accept that no functional test could be as convincing as his described capabilities. The examination reveals no heart strain whatsoever. Besides no asymmetry is noticeable on the thorax.

In other cases we should resort to thoracoplasty sooner or later but we believe that no thoracoplasty after resection should be undertaken until the cardio-respiratory function tests pointing to cor pulmonale or dangerous emphysema make the operation mandatory. We believe that this necessity in most cases can be determined after the operation and not at the same time to avoid a damage that could not present itself afterwards. To this, tuberculosis is an exception, and we realize the importance of the thoracoplasty in this disease to prevent empyema. Also we know that the excision of pleurae at the same time with thoracoplasty in resection is perhaps the best means to avoid empyema.

But when one is dealing with diseases other than tuberculosis there is always time to undertake thoracoplasty under better conditions than immediately after resection.

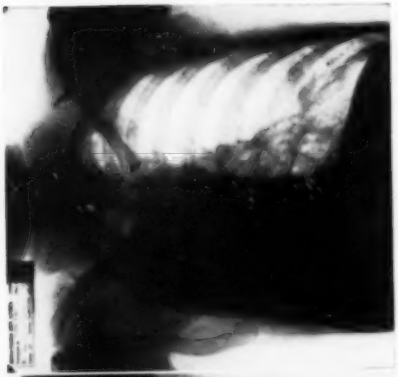

FIGURE 3

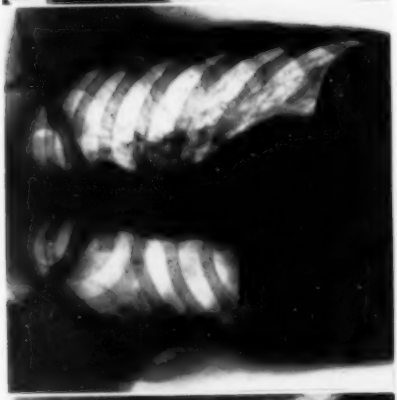

FIGURE 2

FIGURE 1

A man (L. Coronado) of 58 years, over 200 lbs. in weight, came to us with a lung abscess on the left side. Three pneumonotomies had been done before to overcome the suppuration, with only temporary relief each time. Large cavities developed near the initial one and the lung appeared completely destroyed.

Two years ago a total pneumonectomy with total pleurectomy and pericardiectomy on account of short stump was performed. The post-operative period was exceptionally stormy.

He developed cerebral embolism, with hemiplegia and aphasia and a few days later, embolism of the mesenteric artery with large loss of blood through the intestine, the hemorrhage being of about a quart every day, which was replaced every day through the jugular vein until the hemorrhage subsided. No abdominal operation could be attempted in his critical condition for ten days.

However, he recovered from the two embolisms and was able to undergo a thoracoplasty two months later and he is at the present time leading a perfectly normal life (Figure 4).

In this case the thoracoplasty was undertaken on account of the apparent dispnoea that the displacement of the mediastinum was provoking.

Other cases should be dealt with by other procedures as in young people or in women who object to a deforming operation.

Another man (L.C.) of 35 years, was operated on account of carcinoma of the right lower lobe. Pneumonectomy was performed and a rather

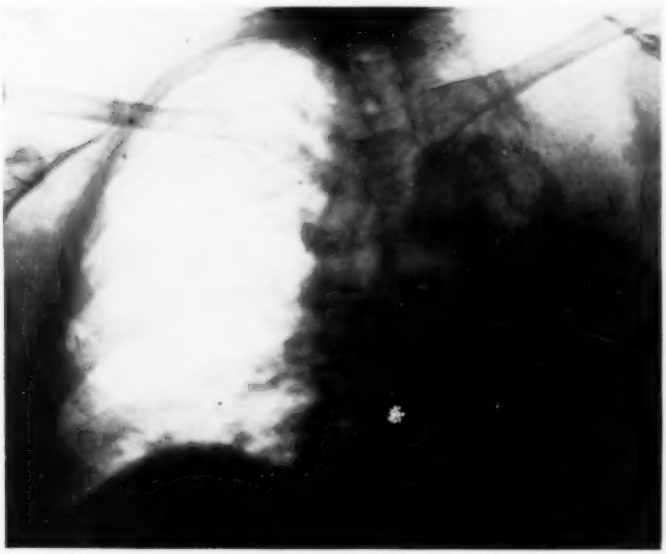

FIGURE 4

malignant type of cancer was diagnosed although no metastases were discovered in the glands or elsewhere.

Thoracoplasty was refused and not considered indispensable; besides, the condition of the patient was not good enough to warrant another operation. The space was filled with celluloid balls which were fairly well tolerated. As the balls occupied the pleural space some pain was expected, but as time passed the foreign material is well tolerated (Figures 5 and 6).

A woman (D.G.), 40 years old, had an intrapleural pneumothorax to close a large cavity without satisfactory results although the lung was liberated from the apex by an open thoracotomy. Pneumonectomy was done and about one month afterwards the space was filled with celluloid balls. For over one year she has been in good condition. The other side however had a flare up but gradually the shadows cleared and now she is almost free of symptoms and the roentgenological appearance is almost normal. The sputum is negative (Figures 7 and 8).

There are other procedures which have been satisfactory in the hands of others and we shall attempt some in appropriate cases:

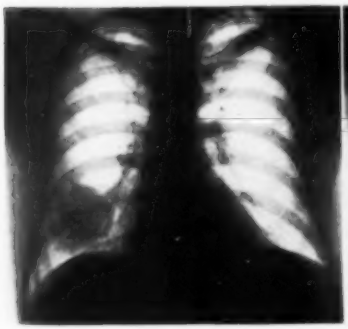

FIGURE 5

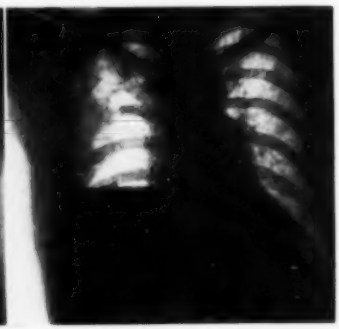

FIGURE 6

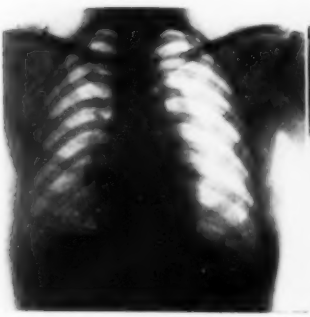

FIGURE 7

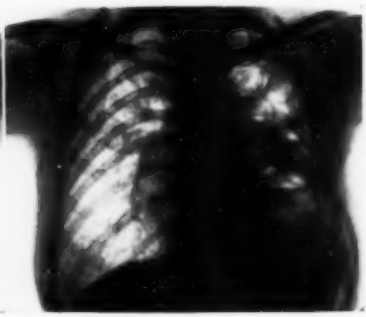

FIGURE 8

Examples are, the use of lucite balls, plastic sponge fillings, and oleothorax.

The Short Stump in Pneumonectomy

By a "short stump" we refer to the situation when the hilum is invaded by fibrous reaction in cases of suppuration or cancer. Invasion by the neoplasm itself is another cause. In tuberculosis this shortening of the accessible hilum is exceptional.

When the structures of the hilum cannot be dissected out on account of this circumstance it was customary to abandon the operation or to try a mass ligature with rather poor results in the immediate postoperative period. In some cases we have attempted to force the procedure and in a few the result was fatal on account of hemorrhage.

The invasion reaches sometimes to the pericardium and we have undertaken the ligation within the pericardium itself in three cases with gratifying results. Ligation of the veins is much easier within the pericardium and the danger of cutting through diseased tissue is lessened.

A man (J. Garcia) 50 years old, had a carcinoma in the lower lobe of the right side. The diagnosis was confirmed by Papanicolaou. The resection seemed to be easy or at least without incidents. However the tumor had already invaded the pericardium in a large measure and we did not even contemplate to resect by the usual approach.

A window was opened in the pericardium of about 6 cm. in diameter and the veins were ligated very easily by this approach. The remainder was ligated in the conventional manner.

This window was left open and a thoracoplasty was done soon after the operation to prevent cor pulmonale. As a matter of fact, he already had signs of cor pulmonale by electrocardiogram.

He has resumed his usual occupation and has only a moderate dispnoea on exertion (Figures 9 and 10).

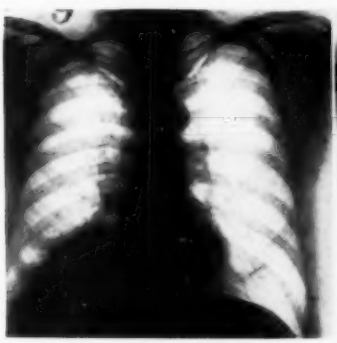

FIGURE 9

FIGURE 10

The Contralateral Spread or Flare-up

Very often we have the problem of the bilateral disease and the attitude is apt to be discussed at length.

Almost all patients who come to us have been treated with streptomycin. It is well known how different is the outcome when bacteriologic resistance has developed and we have been repeatedly advocating the necessity of abstaining from the use of streptomycin indiscriminately when a surgical procedure is contemplated as the necessary step in the near future.

Streptomycin and PAS however are our main weapons to fight

FIGURE 11

FIGURE 12

FIGURE 13

FIGURE 14

the contralateral spread, and an example is the one already presented.

A lady (B.P.) was operated by us about 13 years ago for an apical cavity. Upper thoracoplasty was done with excellent results. She became persistently negative for several years and was lost sight of for some years and we only knew that she married, had a very strenous life and came back after 12 years with evidence of relapse on the same side. Tomography showed three cavities. The older open and two more. Pneumonectomy was performed and after being treated for a bronchial fistula by reoperation she became negative again. However she developed two years later, a new lesion on the opposite side.

A cavity could not be detected but tomography showed the presence of two cavities. Extrapleural pneumothorax was performed on the left side and the appearance soon after the operation is as seen on the tomograms.

We believe that the tolerance of the remaining lung is incredibly good in some cases. This is an example of how far our efforts can go to salvage some of the otherwise desperate cases (Figures 11, 12, 13 and 14).

SUMMARY

The problem of the residual cavity after pulmonary resection is discussed. Examples of cases which do not need any additional procedure, when the remaining lung expands satisfactorily and the space is filled by the mediastinal structures and the lung itself are presented. Post-resection thoracoplasty is also discussed and it is claimed that usually it is not necessary to do this operation immediately after resection. Delayed thoracoplasty is preferred if at all. In other cases delayed filling of the space is advocated by means of material like celluloid balls or plastics. The "short stump" in pneumonectomy, particularly in cancer, is considered as a problem which can be dealt with by isolating the large vessels within the pericardial sac.

Examples of each procedure are given. Also the controlateral spread is presented as the most dreadful complication. The treatment of the remaining lung when the disease takes a destructive appearance, should be the collapsing procedures with the pertinent limitations.

An example of extrapleural pneumothorax on the left side after total pneumonectomy on the right is presented.

RESUMEN

Se discute el problema de la cavidad residual después de la resección pulmonar. Se presentan ejemplos de los casos que no necesitan ningún otro procedimiento adicional cuando el pulmón restante se expande satisfactoriamente y el espacio es ocupado por los organos mediastinales y por el mismo pulmón restante. Se discute la toracoplastia post-resección y se sostiene que habi-

tualmente no es necesario hacer esta operación inmediatamente después de la resección. La toracoplastía tardía si acaso se necesita es preferible. En otros casos se aconseja que se haga más tarde el llenado del espacio por medio de material como las esferas de celuloide o substancias plásticas. El "muñón corto" en neumonectomía, especialmente en cancer se considera como un problema al que se puede hacer frente mediante el aislamiento de los grandes vasos dentro del saco pericárdico.

Se muestra cada procedimiento con ejemplos. También se presenta la diseminación contralateral como la más temible complicación. El tratamiento del pulmón restante cuando la enfermedad toma un aspecto destructivo debe consistir en los métodos de colapso con las limitaciones pertinentes.

Se muestra un ejemplo de neumotorax extrapleural izquierdo después de neumonectomía total en el derecho.

RESUME

L'auteur discute le problème de la cavité résiduelle après résection pulmonaire. Il présente des exemples de malades qui n'ont pas eu besoin de technique particulière dans ce but, c'est qu'alors la partie restante du poumon a subi une bonne expansion et que l'espace s'est comblé grâce au médiastin mobile et au poumon lui-même. Il discute la thoracoplastie systématique après exèrèse. Il montre qu'il n'est en général pas nécessaire de pratiquer cette intervention immédiatement après. On doit donner la préférence dans presque tous les cas à la thoracoplastie secondaire. Dans d'autres cas, l'auteur conseille le comblement ultérieur de l'espace au moyen de billes de celluloid, ou d'un autre materiel plastique. "L'exiguité du moignon" au cours de la pneumonectomie spécialement en cas de cancer peutêtre combattue en isolant les gros vaisseaux à l'intérieur du sac péricardique.

L'auteur montre quelques exemples de chaque procédé. Il insiste également sur l'ensemencement contro-latéral, complication la plus redoutable. Le traitement de l'autre poumon, lorsque des cavités s'y développent, peut se faire grâce à une collapsothérapie limitée.

L'auteur montre un exemple de pneumothorax extra-pleural du côte gauche après pneumonectomie totale à droite.

Discussion

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The problems which have confronted Dr. Alarcón are the same ones which have annoyed us. Furthermore, his solutions to these problems are similar to ours.

There are, perhaps, no rigid rules for the management of the pleural space after pneumonectomy. We have learned that some of ours like Dr. Alarcón's patients, can tolerate a great deal of overdistention, while others cannot. In general it is probably safe to say that the dynamics are disturbed most when mediastinal shift follows right pneumonectomy, and that young, small, flat-chested patients tolerate over-distention better than old, thick-chested, emphysematous patients.

The life-expectancy of patients with carcinoma is such that the secondary thoracoplasty may be postponed justifiably, or the pleural cavity managed by methods already referred to; but in tuberculosis, when a prolonged and good result may be expected, the thoracoplasty should follow the resection by approximately one month to six weeks.

I also agree with Dr. Alarcón that pericardial resection is occasionally necessary in pulmonary resections for tuberculosis, and quite frequently in cases of carcinoma. In general, however, the postoperative course is much more benign if the pericardium is left intact. In a series of more than 50 patients, we have had arrhythmias in 50 per cent of the cases. Some of them have been quite serious and difficult to manage. We no longer do pericardial resection in patients with carcinoma unless it is absolutely essential. Our recurrences have rarely been in the heart or pericardium and routine pericardial resection in carcinoma has proved dangerous in our hands.

Contralateral spread is less frequent now than in previous years, because we isolate, clamp, and divide the bronchus before we compress, squeeze, and dislocate the lung in all four directions. Furthermore, with streptomycin and para-aminosalicylic acid, the patients are better prepared and have much less sputum which contains only relatively few organisms and these are stunned, or perhaps incapable of reproduction, because of the antibiotic therapy. In over 200 consecutive cases of segmental resection, we have had less than four spreads (2 per cent).

Hemothorax Following Incomplete Reexpansion of the Lung After Artificial Pneumothorax

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Three cases of spontaneous hemothorax following incomplete reexpansion of the lung after artificial pneumothorax in arrested pulmonary tuberculosis are presented. They were identical in character and onset. They must constitute a definite entity, since we were able to collect these three cases in less than two years and the background and time relationships in all the cases were strikingly similar.

Waring[1] in a complete discussion of the problem of spontaneous hemopneumothorax in clinics used a table listing in detail the many causes of bloody effusions with and without concomittant pneumothorax.

I. Bloody effusions without pneumothorax
- (a) Malignant disease
  1. Primary pleural
  2. Secondary to malignant disease in:
     - (a) Lung
     - (b) Elsewhere
- (b) Infections
  1. Tuberculous
  2. Fungus
  3. Sepsis
- (c) Acute rheumatic fever
- (d) Blood dyscrasias, especially Leukemia
- (e) Deficiency diseases, especially Scurvy and Beri Beri
- (f) Rupture of syphilitic aneurysm of Aorta
- (g) Rupture of dissecting aneurysm of Aorta
- (h) Rupture of coarctation of Aorta
- (i) Cirrhosis of liver
- (j) Nephritis
- (k) Pulmonary infarction
- (l) Traumatic
- (m) Rupture of bronchus
- (n) Periarteritis nodosa

II. Bloody effusions with pneumothorax
- (a) Ideopathic spontaneous hemopneumothorax
- (b) Tuberculous hemopneumothorax
  1. Spontaneous (perforation of caseous tubercle or tear of adhesions)
  2. A complication of artificial pneumothorax
- (c) External violence
- (d) Miscellaneous

Jones and Gilbert[2] and Koro[3] emphasized a definite clinical syndrome for spontaneous pneumothorax:

1. Sudden severe pain in the chest plus dyspnea. (This is taken as evidence of spontaneous pneumothorax).
2. Temporary improvement, lasting several days. (This is evidence that the pleura has become accustomed to the contained air).
3. Recurrence of pain and dyspnea and the appearance of signs of hemorrhage. (This is evidence of internal pleural hemorrhage).

Our cases had none of the above symptoms and would have been missed entirely except for routine x-ray check-up followed by diagnostic aspiration.

Hartzell,[4] in an excellent review of non-tuberculous hemopneumothorax, stated that in tuberculosis the hemopneumothorax occurs when the disease is both obvious and advanced and cases where the tuberculosis is not obvious or easily discovered at the time of the episode of bleeding may be confidently considered non-tuberculous.

Although our cases all had tuberculosis, the disease was arrested, sputa were and have since remained negative for tubercle bacilli as have the hemorrhagic pleural effusions on many laboratory examinations.

It should be noted, however, that Beatty[5] reported a case of a 20 year old Negro male who had NO disease on the side of the hemothorax although the other side was involved and four months later developed caseous pneumonic disease with cavitation. Birch[6] reported a fatal case of hemopneumothorax where a minute tuberculous cavity was found at the apex of the homolateral lung at postmortem. The cavity wall was intact and the source of air and blood was not identified but there was a "roughened area" on the pleural surface.

Many cases of hemothorax occurring on the side of pneumothorax treatment have been described such as those by Wiener and Jackson,[7] Heise and Krause[8] and also by Hartzell.[4] In our cases, however, pneumothorax had been long discontinued and there had been no needling of the chest either for the purpose of refill or diagnosis prior to the occurrence of the hemorrhagic effusion. Thus, the element of accidental trauma cannot be introduced in these cases.

In recent years the major portion of literature relating to hemothorax has emphasized the traumatic form.[9-11] We could find no objective evidence of trauma such as fractured ribs or any historical evidence other than bicycle riding in case 1 and excessive drinking in case 2. Bernstein, Klosk and Parsonett[12] state that all spontaneous hemothoraces have their origin in the rupture of vascular adhesions, either by a simultaneous spon-

FIGURE 3

FIGURE 2

FIGURE 1

taneous pneumothorax or by an extreme effort in which a vascular adhesion is severed without the occurrence of pneumothorax. They state further, that those cases where the pneumothorax was due to rupture of blebs or cysts resulting from acquired pulmonary disease (as contrasted to congenital), the blebs were found in areas of scar tissue originating from previous parenchymal disease. Although parenchymal disease was considered primary, the bleeding was considered pleural rather than pulmonary in origin because:

1. "The intrapulmonic arterial pressure in the branches of the pulmonary artery is only one-sixth that of the systemic blood pressure, so that bleeding would cease with only a small rise in intrapleural pressure.
2. That when the severed adhesions are examined at autopsy, the proximal segment retracts toward the lung and the bleeding point lies in the distal segment."

In our cases, although we consider the source of bleeding to be pleural, there was no evidence of acquired bleb formation and no evidence for rupture of a vessel by the breaking down of a subpleural tubercle. (No tubercle bacilli were found in the hemorrhagic effusion, early or late).

The case summaries are complete but have been abbreviated for purposes of clarity.

Case 1: H.S., a 40 year old Puerto Rican male, was admitted to Harlem Hospital on March 22, 1942 for active pulmonary tuberculosis. Right pneumothorax was started at that hospital and the patient signed out A.O.R. on April 6, 1942. He was admitted to Metropolitan Hospital on April 23, 1942, where treatment was continued until he was discharged to the clinic on October 22, 1942 as an arrested case. The pleural space was almost dry and 90 per cent collapse of the lung was present. Refills were given at the clinic to January 1947 when the lung was allowed to reexpand. Sputa were negative during the entire course in the clinic. On October 10, 1947 there was noted obliteration of the pneumothorax space with some fluid at the periphery of the right thoracic cage, deviation of the trachea to the right and moderate aeration of the right lung (Figure 1). On January 9, 1948 marked reaccumulation of fluid was noted in the right pleural space. He had no complaint but on questioning stated that he had exerted himself more than usual by riding a bicycle. He was tapped and the specimen disclosed brownish material consisting of old blood and flakes of fibrin but no evidence of tubercle bacilli. Two further taps since that date have shown no change in the character of the fluid but on later taps the fluid could not be removed in quantity. All fluid specimens and sputum specimens have been negative for tubercle bacilli to date. There has been a slow reaeration of the right lung.

Case 2: A.S., a 27 year old Puerto Rican male, was discovered to have tuberculosis in August of 1943 when he went to the Harlem Clinic because of general malaise. He was sent to Bellevue Hospital where right pneumothorax was started in October of 1943. After remaining at Bell-

evue Hospital for eight months, he was sent to Sea View Hospital where he remained for nine months and then was discharged to the clinic for continuation of pneumothorax treatment. He then had approximately 70 per cent collapse of the right lung. Sputa remained persistently negative and the lung was allowed to reexpand. The patient started on "training" for a new trade and was studying four hours daily and felt well. X-ray film of December 29, 1948 (Figure 2) showed almost complete reexpansion of the right lung, deviation of the trachea to that side and a thin layer of pleural fluid. Because of an episode of hemoptysis in March 1949, a film was taken and massive pleural effusion was found. Questioning revealed no evidence of strain or trauma, but the patient is known to occasionally "indulge" in alcohol. He was tapped and brownish, non-clotting fluid was removed. This contained old blood, no tubercle bacilli or tumor cells. Four months later the status was unchanged except for some reaeration of the right lung (Figure 3). Slow reexpansion has continued to date but fluid removed on August 25, 1950 was now found to be clear and yellow which indicated the transition from a hemorrhagic to a serous effusion. Sputa and fluid have remained negative for tubercle bacilli.

Case 3: A. de T., a 24 year old Puerto Rican female, had the onset of her tuberculosis in 1942 marked by an episode of hemoptysis. After a short stay at Kings County Hospital she was transferred to Seton Hospital where left pneumothorax was started. The patient was discharged as arrested after one year but went to Sea View Hospital six months later because of hemoptysis. Pneumothorax was maintained and she was discharged to the clinic as an arrested case. In October of 1948, in the eighth month of pregnancy, pneumothorax was abandoned. The x-ray film at that time showed a dry left pleural space and 75 per cent collapse of the left lung. On April 20, 1949 the x-ray film showed moderate reexpansion of the left lung, obliteration of the pneumothorax space with a small amount of pleural fluid remaining (Figure 4). In January of 1950, marked reaccumulation of fluid was noted. This was found to be brownish fluid

FIGURE 4

containing blood, flakes of fibrin with no tubercle bacilli or tumor cells seen. Present status is unchanged except for slight reaeration of the right lung.

Discussion

In the foregoing cases there had been a "normal" course of pneumothorax treatment, not complicated by surgical intervention, effusion or reactivation. The cases had been carried on for the "usual" duration of therapy and had "almost" reached the usually desirable optimum result of complete reexpansion of the previously collapsed lung. For no obvious reasons, such as trauma (accidental) or needling, there was found the occurrence of massive accumulation of blood in the pleural space. This was not accompanied in any case by subjective symptoms described in the "definite" clinical syndrome by Jones, Gilbert and Korol. In no case were we able to prove the concomittant occurrance of pneumothorax. The cases were all well controlled as far as tuberculous disease at the time of the hemorrhagic effusion.

The occurrence of this effusion has had no deleterious effect as far as control of disease is concerned, although there has no doubt been a decrease in ventilatory capacity as a result of both decreased pulmonary capacity and pleural fibrosis. It is assumed that the accumulation of bloody effusion in the pleural cavity was brought about by the pronounced intrapleural negative pressure. The latter resulted from the incomplete reexpansion of the lung after discontinuance of artificial pneumothorax.

SUMMARY

1) We have listed three hemopneumothoraces following apparent reexpansion of pneumothorax.

2) The theoretical considerations offered to explain hemopneumothoraces have been listed.

3) Incomplete reexpansion of the lung treated with pneumothorax is a possible cause of hemopneumothorax.

RESUMEN

1) Tenemos anotados tres hemoneumotórax que siguieron a la reexpanción aparente del neumotórax.

2) Las consideraciones teóricas ofrecidas para explicar hemoneumotórax han sido anotadas.

3) La reexpansión incompleta del pulmón tratado con neumotórax es una causa posible de hemoneumotórax.

RESUME

1) L'auteur à constaté dans trois cas l'existence d'un hémothorax à la suite de la réexpansion du poumon traité par pneumothorax.

2) Il expose les considérations théoriques qui peuvent expliquer cette complication.

3) La réexpansion incomplète du poumon soumis à un pneumothorax est la cause possible de ces épanchements hémorragiques intra-pleuraux.

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Emphysematous Bullae and Pulmonary Tuberculosis*

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Dayton, Ohio

1) *Introduction:* The coexistence of two disease processes in the same patient or in the same organ provides some of the most interesting and most difficult problems in diagnosis and treatment. Pulmonary tuberculosis and pulmonary emphysema may be related in a number of different ways; this presentation deals with the development of pulmonary tuberculosis in an area of the lung which is the site of pre-existing emphysematous bullae. The combination of the two conditions in the same lobe or lung presents certain x-ray changes which may offer difficulties in diagnosis, particularly when it is necessary to evaluate the presence and extent of cavitation. A fairly thorough review of the medical literature has led us to the conclusion that this radiological picture has not been described previously.

2) *Definition:* Emphysematous bullae are air-containing spaces within the lung substance which are due to the rupture and fusion of a number of alveoli. They are not lined by epithelium but by compressed alveolar walls or by a thin layer of fibrous tissue. Emphysematous blebs are air-containing spaces between the lung and the pleura, the pleura having been elevated by the air leaking from ruptured alveoli situated upon the lung surface. While both bullae and blebs may occur at any age they are most commonly in evidence on x-ray films of middle-aged males who have coincidental bronchitis, asthma or generalized emphysema. It is important that they be distinguished from pulmonary cysts, which are usually developmental anomalies. Cysts have distinct fibrous tissue walls and columnar or cuboidal epithelial lining and usually have a fairly direct communication with the larger branches of the bronchial tree.

3) *X-ray Appearances:* (A) The typical appearance of a bleb

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or bulla appearing at the apex of the lung consists of an oval area of increased radiolucency of varying size, from a diameter of a few centimeters to one-half or more of the lung field. Radiologic differentiation between blebs and bullae is usually difficult and no such distinction will be attempted in this study. The bulla itself contains no lung markings, but these may show through from pulmonary tissue anterior to or posterior to the bulla. This is especially true when such bullae are present at the lung base or at the free mediastinal border of the lung. The blebs or bullae may be multiple and then present linear shadows within them. These are usually at right angles to the pleural margin and represent inter-bullar septa. The pleural margins are usually thin and do not give the appearance of "thickened pleura." The pulmonary margins may be sharp, suggesting a well-formed wall but are often quite indistinct so that the exact medial limiting border may be impossible to localize. Emphysematous bullae are usually seen to be stationary on serial chest x-ray films or may gradually increase in size over a period of years. They rarely decrease in size or disappear completely.

(B) The development of tuberculosis in a lobe containing bullae presents a bizarre picture. The bullae themselves remain radiolucent but the adjacent infiltration may progress into the inter-bullar septa or into lung tissue lateral, medial, anterior or posterior to the bullae. The x-ray appearance may then simulate that of caseous pneumonia which has undergone extensive excavation. Figure 1 illustrates lung fields which were known to be the seat of bullae for many years before the onset of pulmonary tuberculosis. Bullae were present equally in both upper lobes. When the tuberculosis in the right upper lobe became sufficiently extensive it could only be distinguished with difficulty from caseous pneumonia with numerous large cavities. In the absence of earlier films the numerous air-containing spaces would probably have been interpreted as giant cavities, giving rise to a false estimate of the actual pathologic changes.

We have observed five instances in which active tuberculous infiltrates appeared in lung areas containing large emphysematous bullae. Two of these resolved with rest alone, one necessitated thoracoplasty (with subsequent clinical arrest), and two have remained active and progressive. From this scant experience it would appear that the presence of tuberculous infiltration in a bulla-containing lobe is neither necessarily benign nor of extremely grave significance.

(C) Fluid levels in emphysematous bullae: Six instances were observed in which pre-existing bullae developed fluid levels. In four cases this finding accompanied or followed the obvious de-

velopment (as seen upon x-ray films) of a tuberculous infiltrate in an adjacent area of lung tissue. In two other cases the patients were thought to have had inactive pulmonary tuberculosis (in each instance contralateral thoracoplasty was present) when upon a routine chest x-ray film the fluid level was seen in a pre-existing bulla. In neither case did this development have any apparent ultimate untoward significance. Both patients were clinically well and asymptomatic at the time of this finding. In each, however, previously negative sputa became positive for tubercle bacilli upon culture and remained so for several months. No tuberculous infiltrate could be identified on x-ray films in subsequent months but the development of sputum cultures positive for tubercle bacilli presumably indicated an active tuberculous focus in the juxta-bullous lung tissue. In almost every case where a fluid level was observed to develop in an emphysematous bulla, the bulla gradually shrank and disappeared leaving at most a linear shadow suggesting fibrosis. In none of the patients with active tuberculosis was there any evidence that this development had any harmful effect upon the disease. No new symptom appeared and the disease followed a course about as might have been expected in the absence of this complication. A few illustrative cases are cited.

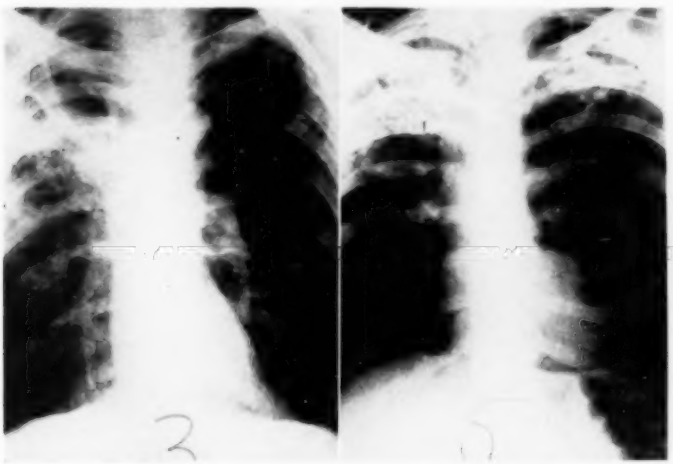

FIGURE 1 FIGURE 2

Figure 1, Case 1 (January 21, 1946): Bilateral upper lobe emphysematous bullae had existed for at least 8 years prior to this x-ray film. When pulmonary tuberculosis developed the inflammatory process involving the interbullar septa simulated huge cavities. — *Figure 2, Case 1* (July 9, 1946): Numerous fluid levels can now be seen in the left upper lobe with infiltration in the adjacent lung tissue.

Case 1: This man was born in 1894. He was diagnosed as having asthma and his chest x-ray films revealed bilateral upper lobe bullae from 1938 to 1944. Pulmonary tuberculosis appeared in the right lung in January 1946 (Figure 1), the left being unchanged. Infiltration then developed in the left upper lobe, as seen upon an x-ray film of July 9, 1946, and this was accompanied by the development of multiple fluid levels. Figure 2, made on July 9, 1946, shows a confluent nodular infraclavicular infiltration in the left upper lobe. Multiple fluid levels may be seen in a number of preexisting emphysematous bullae, bearing some resemblance to multiple rapidly developing cavities. This process progressed (Figure 3, August 9, 1946) and regressed (Figure 4, October 30, 1947). Before the lesion resolved completely one apical bulla cleared and redeveloped fluid on one occasion. The left upper lobe lesion then became inactive in that evidence of tuberculosis receded and the bullae gradually disappeared, perhaps because of inflammatory obliteration of their alveolar or bronchial communications. In December 1947 right thoracoplasty was performed. In August 1948 he was clinically inactive with negative sputum cultures. The left lung presented a faint semicircular line (not illustrated) with concavity inward towards the hilum. This had been present for a number of months at least and was subsequently interpreted as the outer margin of an emphysematous bulla at the anterior mediastinal free border of the left upper lobe. Routine x-ray film (Figure 5, September 15, 1948) revealed the bulla to be half-filled with fluid. There was no new symptom at this time, such as fever or increased expectoration, but two sputum cultures were found positive for tubercle bacilli. In subsequent months the bulla shrank and disappeared. All

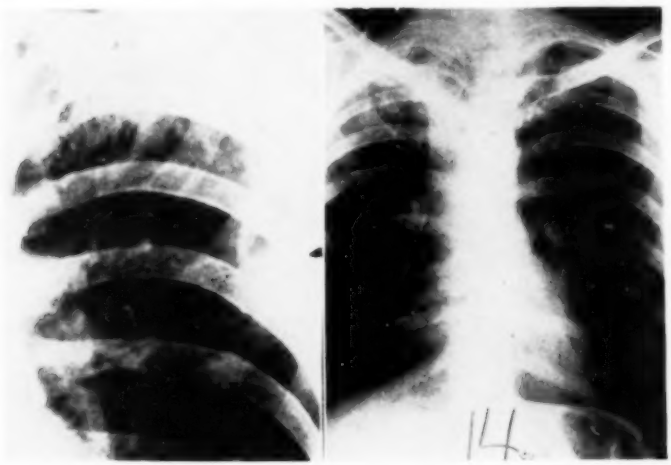

FIGURE 3 FIGURE 4

Figure 3, Case 1 (August 9, 1946): A new, previously uninvolved area at the apex of the left axilla now also presents a fluid level.—*Figure 4, Case 1* (October 30, 1947): Complete disappearance of the left upper lobe bullae and fluid levels. Note also the marked contraction of the right upper lobe lesion with obliteration of the bullae.

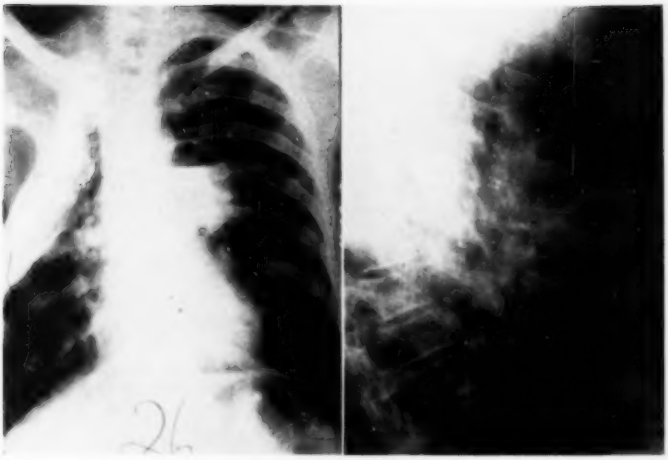

FIGURE 5. Case 1 (September 15, 1948): Postero-anterior and lateral films showing a fluid level in a bulla located at the anterior mediastinal border of the left lung.

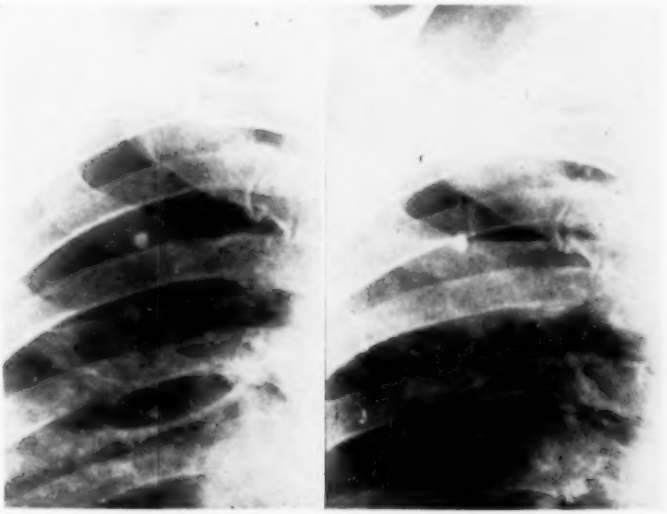

FIGURE 6

FIGURE 7

Figure 6, Case 2 (December 4, 1946): Detail of right upper lobe. The lung field is occupied by a bulla measuring 12 x 8 cm. Lung markings can be seen through the bulla.—*Figure 7, Case 2* (August 9, 1950): Routine x-ray film revealed fluid level. There was no symptom or new evidence of active tuberculosis but three sputum cultures were positive for tubercle bacilli.

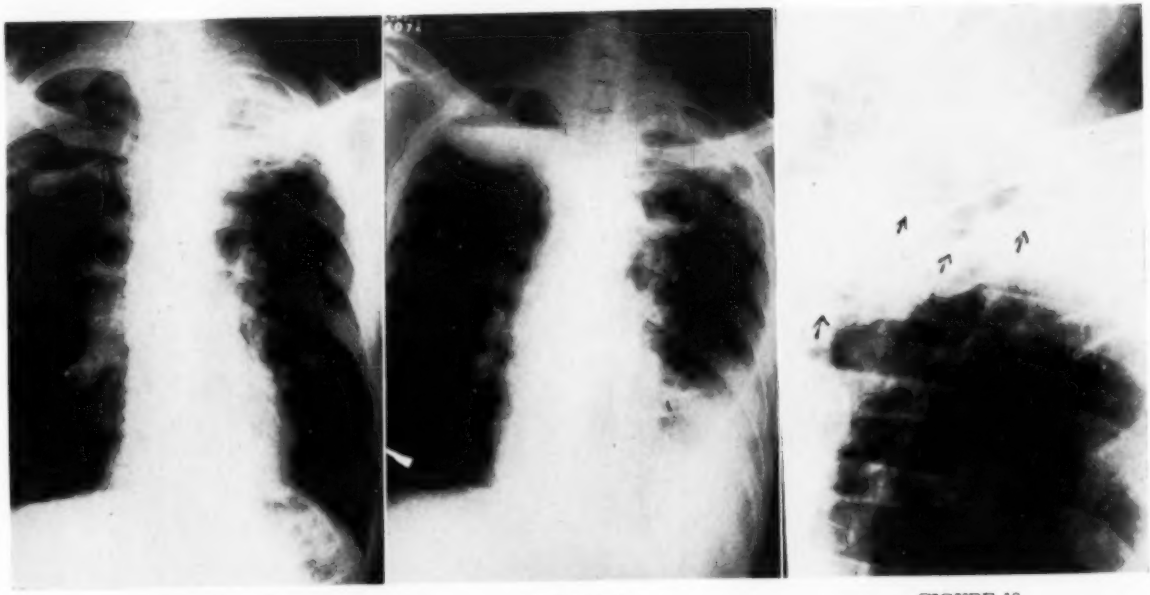

FIGURE 8 FIGURE 9 FIGURE 10

Figure 8, Case 3 (December 5, 1949): A large bulla (10 x 6 cm.) is present in the right upper lobe. Active tuberculosis is present on the left and probably in the juxta-bullous portion of right upper lobe.—*Figure 9, Case 3* (March 2, 1950): The fluid level can be seen in the right upper lobe. The disease on the left has progressed.—*Figure 10, Case 4* (April 8, 1949): Detail of left upper lobe showing multiple fluid levels. Bullae only were seen in this area on a previous x-ray film of December 28, 1948.

sputum and gastric cultures were negative after July 1949 and he was discharged as an arrested case in September 1950.

Case 2: This man was born in 1896 and had a long history of asthma and chronic bronchitis. Chest x-ray film, made in 1938, revealed evidence of far advanced pulmonary disease which proved to be tuberculosis, confined to the left upper lobe. The right upper lobe presented evidence of emphysematous bullae but no tuberculous infiltrations could be visualized. The far advanced active pulmonary tuberculosis on the left was treated with thoracoplasty in 1939. The right upper lobe first showed evidence of active tuberculous infiltration in the area adjoining the bullae in 1944. X-ray film of October 7, 1944 (not shown) revealed a fluid level in one of the bullae. He was treated with bed rest alone; the fluid level soon disappeared but the bulla persisted and by 1946 the pulmonary lesion became arrested by x-ray criteria (Figure 6, December 5, 1946) and negative sputum cultures. The disease remained inactive by these criteria for the following four years. On August 9, 1950, a routine x-ray film revealed the bulla to be partly filled with fluid (Figure 7). There were no increased cough, fever, hemoptysis or other new symptoms. Sedimentation rate was 10 mm. in 1 hour. Nine sputum cultures and two gastric cultures were negative for M. tuberculosis but three sputum cultures were positive. Serial x-ray films showed the lesion gradually shrinking so that by January 1951 the bulla and fluid had both been lost to view, leaving no x-ray evidence of a new pulmonary infiltrate. Subsequent sputum and gastric cultures were negative for tubercle bacilli.

Case 3: This man was born in 1894 and had a history of asthma dating to 1935. A chest x-ray film made in 1939 was negative for pulmonary tuberculosis but revealed bilateral apical emphysematous bullae. Left-sided pleurisy developed in 1943 and spontaneous pneumothorax on the right side in 1946. Chest x-ray film at that time revealed far advanced tuberculosis in the left upper lung field. The right lung presented no radiological evidence of tuberculosis. The disease slowly progressed but remained confined to the left lung until December 1949, at which time some scattered infiltration was seen upon the right. At this time an x-ray film (Figure 8, December 5, 1949) revealed the emphysematous bulla to have enlarged, suggesting positive pressure within it. Another x-ray film (Figure 9, March 2, 1950) showed the bulla partly filled with fluid. There was no new clinical finding at this time, such as fever, or increased expectoration. The subsequent course of this right upper lobe lesion has consisted of gradual decrease in size of the fluid-filled bulla, with increasing infiltration in the adjacent lung field.

Case 4: This man was born in 1890 and had a long history of chronic bronchitis and asthma. Pulmonary tuberculosis had been present since 1941. The lesion was largely confined to the right upper lung field. Emphysematous bullae could be seen in the left upper lobe. A routine x-ray film (Figure 10, April 8, 1949) revealed multiple fluid levels in the left upper lobe bullae. There was no new symptom associated with this development. Subsequent chest x-ray films gradually showed absorption of air and fluid and disappearance of the bullae.

Case 5: This man was born in 1895 and had a long history of "chronic bronchitis." A chest x-ray film on June 8, 1948, revealed a dense caseous pneumonic lesion in the right upper lung field. Sputum examinations were positive for M. tuberculosis. The left lung revealed a curvilinear

shadow, semicircular in shape, with its concavity in the region of the hilar shadow. A routine x-ray film one month later showed this area to be about one-half filled with fluid. It disappeared quickly and was not seen on subsequent films. The x-ray appearance of this fluid and air-containing bulla was quite similar to that illustrated by Figure 5.

4) *Discussion:* In reviewing the literature, no previous reference was found, nor illustration discovered, dealing with the peculiar behavior of a bulla-containing area which became secondarily tuberculous. Indeed, fluid levels in emphysematous bullae even in the absence of tuberculosis seem quite rare, and unlike epithelium-lined cysts, bullae become infected infrequently.[1]

Although blebs and bullae may occur in individuals of any age group, as evidenced by the common occurrence of spontaneous pneumothorax secondary to such lesions, they are infrequently visualized upon the x-ray films of younger persons. It is not unusual, however, in routine x-ray films of the chests of middle-aged or older men, to see evidence of bullae in one or both apices. While they may be of almost any size, in order to be recognized they must, as a rule, attain a size of 2 to 3 cm. in diameter. They may be unilateral or bilateral. Through the years they may remain stationary or increase in size, gradually or suddenly. While most commonly seen in an apical area they may also be identified at the lung base or adjacent to the mediastinum. When in this latter location a lateral x-ray film usually reveals them to be at the anterior mediastinal free border of the lung. Although the pleural margins are always sharply outlined and convex, conforming to the rib cage, the pulmonary margin varies. In some instances this border may be rather indistinct and poorly outlined, while in others, the inner border is clear and convex, and usually fairly dense. It is felt that the latter condition probably represents a situation in which the air within the bulla is under tension.

The pathogenesis of blebs and bullae has been discussed in the literature.[2-4] It is generally believed that localized air trapping occurs due to bronchial or bronchiolar stenosis with a check-valve mechanism. Rupture and merging of alveoli then result secondary to increasing pressure, and an air space develops. When this air space is within the lung substance proper, it is spoken of as a bulla. When it occurs at the lung surface so that it is subpleural, it is referred to as a bleb. In this presentation we have made no distinction between blebs and bullae, as this is impossible without examination of a removed specimen. As to the etiology of the bronchial lesion postulated as a predisposing cause for the bullae, considerable confusion exists. Many authors speak of tuberculosis as the primary disease but pathological confirmation is totally lacking. It is, perhaps, usual to diagnose upper lobe densities

resembling fibrosis, when seen radiologically, as tuberculous in etiology, but this alone is not sufficient evidence to assign tuberculosis as the cause of the majority of emphysematous blebs or bullae. When these structures have been examined after surgical removal or at autopsy, the descriptions often refer to fibrosis and some non-specific inflammatory process but no pathological reports of tuberculosis as the underlying cause have been recorded in the literature.

All of our cases were in middle-aged men who had a history of "asthma" or "chronic bronchitis." Whether the same process which produces bullae also causes chronic cough, or whether the chronic cough produces the bullae is not certain.

When tuberculosis develops in the juxta-bullous portion of the lung it at first has no distinguishing characteristics, but when the walls of the bullae are involved the radiologic picture is unique, and can give rise to serious errors in the interpretation of the pathologic changes and in prognosis if the true nature of the process is not appreciated. This is particularly true if fluid levels develop in bullae which are then misinterpreted as cavities.

The differential diagnosis between bullae and tuberculous cavities hinges upon several features: (1) If x-ray films were made before pulmonary tuberculosis developed they may reveal the presence of blebs or bullae in the areas under study. This should lead to a correct diagnosis. (2) Emphysematous bullae are commonly bilateral. The presence of bullae in the contralateral lung may give the clue to the atypical appearance of the lesion in the involved lung. (3) The x-ray film appearance of the lesion itself is fairly distinctive. When a rather large tuberculous cavity is immediately subpleural, the pleural margins and cavity walls usually cast a rather thick shadow (2 to 5 mm.) due to pleural and pulmonary changes. The pleural margins and bullous walls of emphysematous bullae are usually thin and sharp. This point alone is often enough to make a differential diagnosis even in the absence of No. 1 and No. 2 in the foregoing. The rapid appearance and disappearance of fluid and air-containing spaces with no symptoms of toxicity or increased expectoration are much more suggestive of this disease complex than of tuberculous cavitation. In our cases the fluid levels usually developed during an interval of a few weeks or months and disappeared just as rapidly, leaving fairly normal lung tissue behind. It is, of course, always possible for tuberculous cavitation to develop in a lobe which is also the seat of emphysematous bullae.

In the two instances studied by us in which the tuberculosis had previously been considered inactive, fluid levels developed in emphysematous bullae. While the true nature of the condition was

eventually appreciated, various other conditions had to be considered. These included carcinomatous abscess, lung abscess, lung cyst, hydropneumothorax, etc. The knowledge of a pre-existing bulla, plus the thin clear walls of the lesion, in the absence of any symptom, should enable an accurate differential diagnosis to be made.

The prognosis of this combination of disease processes cannot be determined by a study of a few cases. In our small group the presence of bullae, as well as the appearance of fluid within the bullae, seemed to have no effect upon the subsequent course of the tuberculous disease. Despite the development of fluid levels the clinical course was unaffected. Fever and increased expectoration were not noted. However, two previously inactive cases had positive sputum cultures for a few months during the evolution of the fluid in the bullae. In the absence of rest treatment further clinical evidence of activity might have developed. The bullae in each case gradually shrank and lost their identity. They were either lost to view or persisted as linear shadows. The tuberculosis pursued a course much as might have been expected in the absence of complicating factors.

Considerable doubt was originally felt as to the possibility of a favorable prognosis when tuberculosis and emphysema coexisted in the same lobe. This was based partly upon the fact that when tuberculosis is present in a pulmonary lobe which is subsequently distended by compensatory emphysema, as may develop after lobectomy or pneumonectomy, an unfavorable course is occasionally observed—apparently due to overdistension. It is, therefore, worthy of note that in several instances in our series the process became clinically arrested when bed rest alone was utilized.

SUMMARY

1) Pulmonary tuberculosis may develop in an area of lung which is the site of pre-existing emphysematous bullae.

2) The combined process may present a bizarre picture suggesting extensive caseation and cavitation.

3) Fluid levels may develop in such bullae, apparently due to tuberculous changes in their walls. It is believed this is a hitherto undescribed disease complex.

4) The presence of bullae apparently has no effect upon the prognosis of the tuberculous process. However, the development of fluid levels in such bullae may be an indication of a spread or reactivation of the tuberculous process in a juxta-bullous location.

5) If the bullae are diagnosed as tuberculous cavities, one may be led to give a falsely poor prognosis or to recommend unnecessary extensive thoracic surgery.

RESUMEN

1) La tuberculosis pulmonar puede desarrollarse en un area del pulmón con ampolla enfisematosa preexistente.

2) El proceso combinado puede presentar un bizarro aspecto sugiriendo caseificación y excavación amplias.

3) Los niveles líquidos pueden desarrollarse en tales ampollas en apariencia, debido a las alteraciones tuberculosas de sus paredes. Se cree que este es por lo tanto un complejo de enfermedad no descrito.

4) La presencia de la ampolla aparentemente no tiene efecto sobre el pronóstico del proceso tuberculoso. Sin embargo, el desarrollo de los niveles líquidos en dicha ampolla puede ser una indicación de la propagación o reactivación del proceso tuberculoso en la misma.

5) Si las ampollas son diagnosticadas como cavernas tuberculosas uno puede ser llevado a efectuar un mal pronóstico falso o a recomendar cirugía torácica innecesariamente extensa.

RESUME

1) La tuberculose pulmonaire peut se développer dans une zone du poumon ou existent préalablement des bulles d'emphysème.

2) La combinaison de ces deux processus peut réaliser que image curieuse qui fait penser à une plage caséeuse étendue, avec excavation.

3) Des niveaux liquidiéns peuvent apparaitre dans de telles bulles, dont uraisemblablement la cause réside dans les altérations tuberculeuses de leurs parois. Les auteurs pensent qu'un tel complexe pathologique n'a jamais été décrit jusqu'à prisent.

4) La présence de bulles n'a probablement pas d'effet sur l'évolution de la tuberculose. Toutefois, l'apparition d'un niveau liquidien dans de telles bulles peut faire penser qu'il existe au voisinage un foyer tuberculeux récent ou une ráactivation.

5) Si ces bulles sont prises à tort pour des cavernes tuberculeuses, on pourrait porter à tort un pronostic défavorable, et recommander une intervention chirurgicale inutile.

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Editorial

CHEMOTHERAPY IN TUBERCULOSIS

Over 7000 years ago in India and 5000 in China, various drugs and concoctions were being administered to consumptives. Throughout the centuries in ancient Babylon, Egypt, Greece and Rome many drugs were in use. Galen (131-200 A. D.) with deep interest in consumption made numerous journeys through the Mediterranean world and never missed an opportunity to inquire after local drugs. One trip to Palestine was for the sole purpose of studying the preparation of pitch. He is now referred to as "one of the most remarkable figures in medical history." For nearly 1500 years after his death he ruled the medical world. Throughout these centuries physicians everywhere prescribed drugs for consumptives as Galen had employed them.

In 1720 Marten said: "Of all the Distempers that afflict Mankind, there's not one for the Cure of which more Remedies have been appropriated and invented than for Phthisis or Consumption of the Lungs." Numerous drugs have been investigated since Marten's time. Chemical reagents were found to destroy tubercle bacilli in vitro but none which would serve as a germicide in human tissues without harm to the recipient.

Hope of finding satisfactory chemotherapeutic agents had been practically abandoned until the early sulfonamides and the first effective antibiotic—penicillin, proved so effective in combating some infections in the late 1930s. Although these drugs do not significantly affect tuberculosis, hope was raised that further exploration in these fields might lead to efficacious drugs for this disease. In rapid succession the sulfones (promin, diasone and promizole), 1940, para-aminosalicylic acid, 1943, and streptomycin, 1944, were announced. Sulfones suppressed tuberculosis in animals and to some extent in man. Although they have been largely superseded by para-aminosalicylic acid and streptomycin they are still being studied and their possibilities probably have not been exhausted. The efficacy of combined intermittent administration of streptomycin and para-aminosalicylic acid is well established. The bacteriostatic effect of these drugs has been a great boon in controlling lesions and markedly increasing indications for excisional surgery. Recent studies have suggested that with prolonged administration these drugs may even be bacteriocidal. If this is not confirmed, the hope is entertained that one or more of the many new drugs being produced will serve this purpose. Isonicotinic acid hydrazide now on trial, has not been in use sufficiently long to justify conclusions concerning its efficacy.

In this issue of *Diseases of the Chest* Colonel Jacobs reemphasizes a long disturbing fact, namely, that in many tuberculous lesions, when first diagnosed their vascularity is so reduced that there is little likelihood of a bacteriocidal drug reaching many of their tubercle bacilli even though it is in adequate concentration in the blood stream.

Although laudible attempts are being made to bring tubercle bacilli from caseous and necrotic areas by potassium iodide, etc., and to introduce drugs directly into cavities, to date it would seem impossible to reach all tubercle bacilli by such methods. In proper dosage tuberculin results in collateral hyperemia; however, there would appear to be little likelihood of restoring destroyed blood vessels. Nevertheless, such procedures are worthy of further trial.

The attack of today and tomorrow must be directed at the tubercle bacillus itself. Removal of clinically involved lungs, lobes, segments and even smaller units is now accomplished by new surgical techniques with considerable safety under the protection of chemotherapy. To date this seems logical treatment. While this prevents some persons from becoming ill and restores others to good health, it does not cure tuberculosis in the strict sense of the word. The person who has necrotic areas, cavities, etc., removed is almost certain to have other tubercle bacilli-bearing lesions. Usually when tubercle bacilli first invade the body they are carried by neutrophils into the blood stream so as to produce bacillemia. They are then promptly focalized at various places where tubercle formations develop. At one or more of these points of focalization sooner or later clinical lesions may appear. One person may have such lesions develop in a kidney, another in a bone or joint, still another in meninges. More such lesions develop in lungs because original focalizations occur there with great frequency. However, the removal of one such lesion under chemotherapy protection does not insure against later evolution of one or more lesions at the original points of focalization both in the lungs and extrathoracically.

By the time a clinical lesion evolves so as to require excisional surgery it is likely that the lesions laid down elsewhere have undergone such changes that their tubercle bacilli cannot be reached by drugs in the blood stream.

Must Diagnose Tuberculosis Early

If our present drugs or those in future use prove to be bacteriocidal they may actually cure tuberculosis if the disease is diagnosed sufficiently early. In most cases diagnoses can be made within two months after bacilli invade the body. The diagnosis is dependent upon conversion of tissues to a state of sensitivity

to tuberculo-protein which is readily detected by the tuberculin reaction. When the individual's tissues first become sensitive to tuberculin and for some time thereafter, the lesions of the primary complexes are small and vascular. Regardless of how many are present or where they are located, a germicide in the blood stream should reach all of their tubercle bacilli with complete sterilization of the body. This is precisely the way we like to treat syphilis. The only reason it has not been employed in tuberculosis has been the lack of a germicidal drug.

With such drugs probably in the offing it behooves every physician to determine the tuberculin status of everyone for whom he is responsible. Those who are nonreactors should be tested periodically and when one converts, drug treatment should be instituted promptly.

In areas where nearly all persons become infected during childhood, all infants should be tested a few weeks after birth and every few months thereafter as long as they are nonreactors. Sterilizing the bodies of those who convert should prevent meningitis, miliary disease, crippling deformities of bones, joints, etc. Should such individuals again become tuberculin reactors, indicating new infections, repetition of chemotherapy would be necessary.

In most parts of the United States more adults than children acquire primary tuberculosis and the tuberculin reaction is dependable at all ages of life to determine if and when infection occurs.

As long as we allow primary infections to go unnoticed and begin treatment after illness appears or lesions are demonstrable by x-ray film inspection, we can hardly expect to cure tuberculosis in the strict sense of the word.

Jay Arthur Myers.

Interim Session

The interim session of the American College of Chest Physicians will be held at the Cosmopolitan Hotel, Denver, Colorado, November 30-December 1, 1952. On Sunday, November 30, the Rocky Mountain Chapter of the College will sponsor a scientific program and on Monday, December 1, the Board of Regents of the College will hold its semi-annual meeting.

Dr. Arnold Minnig, Denver, Governor of the College for Colorado, is serving as chairman of the arrangements committee, and has announced the following program:

SUNDAY, NOVEMBER 30, COSMOPOLITAN HOTEL

Morning Session

Carl W. Tempel, Col., MC, USA, Denver, President,
Rocky Mountain Chapter, Chairman

"Arterio Venous Fistula of the Lung,"
Alfred Goldman, St. Louis, Missouri.

"Cancer Detection in Large City Tuberculosis Surveys,"
Otto L. Bettag, Chicago, Illinois.

"Treatment of Heart Failure,"
John F. Briggs, St. Paul, Minnesota.

"The Surgical Treatment of Mitral Stenosis,"
Alfred N. Goldman, Beverly Hills, California.

Round Table Luncheon Discussions

1) "When Should Artificial Pneumothorax be Terminated?"
Edward W. Hayes, Monrovia, California and
Louis Mark, Columbus, Ohio.
Moderator: Harold M. Van Der Schouw, Wheatridge, Colorado.

2) "Diagnosis and Treatment of Carcinoma of the Lung,"
William A. Hudson, Detroit, Michigan and Seymour M. Farber,
San Francisco, California.
Moderator: John B. Grow, Denver, Colorado.

3) "Management of the Cardiac Patient,"
John F. Briggs, St. Paul, Minnesota, Alvis E. Greer, Houston,
Texas and Alfred N. Goldman, Beverly Hills, California.
Moderator: W. Bernard Yegge, Denver, Colorado.

Afternoon Session

Fred R. Harper, Denver, Colorado, Past President,
Rocky Mountain Chapter, Chairman

"The Pathomechanics and Treatment of So-Called Hypertrophic Emphysema,"
Andrew L. Banyai, Milwaukee, Wisconsin.

"Clinical and Cytologic Findings in Patients Receiving Aerosol Tryptar,"
Seymour M. Farber, Samuel Pfarr, David A. Wood and
R. Daniel Gorman, San Francisco, California.

"Pulmonary Fibrosis with Special Regard to Idiopathic Diffuse Interstitial Fibrosis,"
J. Winthrop Peabody, Washington, D. C. and
J. Winthrop Peabody, Jr., New Orleans, Louisiana.

"The Physical and Physiological Influences in Respiration,"
Burgess L. Gordon, Philadelphia, Pennsylvania.

Evening Session

6:30 p.m. Dinner, J.C.R.S. Sanatorium, Spivak, Colorado, Dr. William Klein, Medical Director.

8:00 p.m. X-ray Diagnostic Conference, Medical Staff.

Dinner by courtesy of the sanatorium.

MONDAY, DECEMBER 1

9:30 a.m. Tour through a modern cardio-pulmonary laboratory, National Jewish Hospital, Dr. Sidney Dressler, Medical Director.

12:00 noon. Luncheon for Board of Regents, American College of Chest Physicians.

Luncheon by courtesy of the hospital.

2:00 p.m. Semi-annual Meeting, Board of Regents, Cosmopolitan Hotel.

19th Annual Meeting Program

Physicians who wish to request places on the Annual Meeting Program of the College, to be held in New York City, May 28-31, 1953, should write to the Chairman of the Committee on Scientific Program, Dr. Arthur M. Olsen, Mayo Clinic, Rochester, Minnesota.

All requests must be accompanied by an abstract as well as the full title of the paper to be presented.

Chest Disease Symposium

Plans for the Fourth Annual Chest Disease Symposium to be given January 22 and 23, 1953, at the Los Angeles County Medical Association Building, 1925 Wilshire Boulevard, Los Angeles, California, are announced by Dr. Thomas H. Sternberg, representing the University of California at Los Angeles, School of Medicine. Co-Chairmen of the Symposium are Drs. Alfred Goldman, Chief of Thoracic Surgery, City of Hope, Los Angeles, and Elliot A. Rouff, Instructor, College of Medical Evangelists.

The course will be sponsored by the UCLA School of Medicine in cooperation with the Los Angeles County Tuberculosis and Health Association, the American College of Chest Physicians, the Los Angeles Trudeau Society, and the Schools of Medicine of the University of Southern California and the College of Medical Evangelists.

Visiting speakers are as follows: Drs. Andrew L. Banyai, President, American College of Chest Physicians and Associate Clinical Professor of Medicine, Marquette University School of Medicine, Milwaukee; Brian B. Blades, Professor of Surgery, George Washington University, School of Medicine, Washington, D. C.; Alvis E. Greer, Clinical Professor of Medicine, Baylor University, College of Medicine, Houston, Texas, and President-Elect, American College of Chest Physicians; H. Corwin Hinshaw, Clinical Professor of Medicine, Stanford University School of Medicine, San Francisco, California; Edgar Mayer, Clinical Professor of Medicine, New York University Post Graduate Medical School, New York; Sidney J. Shipman, President, National Tuberculosis Association, and Clinical Professor of Medicine, University of California School of Med-

icine, San Francisco; and Marcy L. Sussman, formerly Clinical Professor of Radiology, Columbia University College of Physicians and Surgeons, New York City, now Consulting Radiologist, Veterans Administration Hospital, Whipple and Phoenix, Arizona.

Programs and registration information may be secured on request by writing to the University of California Medical Extension, Los Angeles 24, California.

Postgraduate Course in Congenital Heart Disease

The American College of Chest Physicians in cooperation with the College of Medicine of the University of Utah is sponsoring a Postgraduate Course in Congenital Heart Disease. The course will be given at the Salt Lake General Hospital Infirmary Ampitheater, Salt Lake City, Utah, November 19-21, 1952.

Address all inquiries to the Director of the Division of Graduate and Postgraduate Medical Education, University of Utah, 175 East 21st South Street, Salt Lake City 15, Utah. Tuition fee is $30.00.

College Chapter News

SOUTHERN CHAPTER

The Ninth Annual Meeting of the Southern Chapter of the College will be held in Miami, Florida, November 9 and 10, 1952.

A Breakfast Meeting at the Alcazar Hotel will precede the November 9th morning Scientific Session, Dr. Sydney Jacobs, New Orleans, Louisiana, Chairman, Medical Section, will preside. The following papers will be presented:

"The Use of Iso-Nicotinic Acid Derivatives in the Treatment of Tuberculosis,"
Morton M. Ziskind, Emory Calovich, John Joffko and Sydney Jacobs, New Orleans, Louisiana.

"Sarcoidosis: Current Concepts of Etiology and Diagnosis,"
Max Michael, Jr., Atlanta, Georgia.

"The Treatment of Pulmonary Histoplasmosis,"
John H. Seabury, New Orleans, Louisiana.

"The Cardiac Mimics of Pulmonary Disease: Diagnostic Value of Angiocardiography,"
Albert L. Hyman, New Orleans, Louisiana.

A Luncheon Meeting will be held for the Regents and Governors at the Alcazar Hotel. Dr. Edward Parker, Charleston, South Carolina, Chairman, Surgical Section, will preside at the afternoon Scientific Session. The following papers will be presented:

"Resection for Mycotic Pulmonary Disease,"
Felix A. Hughes, Jr., Howard W. Whitaker, Conie C. Lowery, John W. Polk, Frank E. Foley and John R. Fox, Memphis, Tenn.

"Cystic Diseases of the Lung,"
Francis M. Woods, Boston, Massachusetts.

"Right Cardiophrenic Lesions,"
DeWitt C. Daughtry and John G. Chesney, Miami, Florida.

"Partial Thoracoplasty and Suture Constriction of the Upper Lobe in the Treatment of Pulmonary Tuberculosis (Paulino Procedure)," Paul T. DeCamp, New Orleans, Louisiana and Thomas G. Baffes, Chicago, Illinois.

Following the President's Banquet held at 7:30 p.m., will be an X-Ray Conference, moderated by Dr. Duane Carr of Memphis, Tennessee.

On Monday morning, November 10, the Scientific Session will be continued at the Biscayne Terrace Hotel, Miami, Florida, Dr. Duane Carr, presiding. Papers to be presented are as follows:

"Pneumoconiosis in Soft Coal Miners in Alabama," Louis L. Friedman, Birmingham, Alabama.

"Dyspnea of Pulmonary Emphysema," George R. Meneely, Ross C. Kory and Robert A. Goodwin, Nashville, Tennessee.

A Luncheon Meeting at the Biscayne Terrace Hotel, presided over by Dr. Hollis E. Johnson, Chapter President, will precede the afternoon Scientific Session. After a Business Meeting and Report of the Committees there will be an election of officers. Guest speaker, Dr. Amos Christie, Professor of Pediatrics, Vanderbilt University Medical School, Nashville, Tennessee, will give an address entitled "Histoplasmosis."

ROCKY MOUNTAIN CHAPTER

The Annual Meeting of the Rocky Mountain Chapter of the College, was held in the Stanley Hotel, Estes Park, Colorado, on Saturday, September 13, 1952, immediately following the Colorado State Medical Society Meeting.

Seventy-five physicians attended the interesting Scientific Program. Included among the speakers were Doctors Maurice S. Segal, Boston, Massachusetts, Louis F. Bishop, Jr., New York City, and Charles P. Bailey, Philadelphia, Pennsylvania.

At the Business Meeting of the Chapter, the following officers were elected for 1952-53:

Col. Carl W. Tempel, Denver, President
John S. Bouslog, Denver, Vice-President
B. Thomas McMahon, Denver, Secretary-Treasurer.

WEST BENGAL CHAPTER

The West Bengal Chapter of the American College of Chest Physicians was inaugurated in June 1951 in Calcutta, India. The Governor of this new chapter, Dr. P. K. Ghosh, informs us that four important clinical meetings have been held since that time. The subjects of these meetings were as follows:

"Blood Grouping in Pulmonary Tuberculosis," N. Sen, Calcutta, India.

"Value of Tuberculin as a Diagnostic Aid in Detecting Pulmonary Tuberculosis," P. K. Sen, Calcutta, India.

"Absorption of PAS in Blood in Health and Disease," P. K. Ghosh, Calcutta, India.

"Rationale of Pneumoperitoneum in Upper Lobe Lung Disease," K. N. De, Calcutta, India.

College News Notes

Dr. Arthur J. Cracovaner of New York City lectured before a combined meeting of the Sociedad Mexicana de Otorhinolaryngologia y Broncho-esofagologia and La Sociedad Mexicana de Estudios Sobre Tuberculosis y Enfermedades del Aparato Respiratorio in Mexico City, August 19, 1952. He gave demonstrations in bronchoscopy at the Hospital on August 19 and 20.

Dr. Gordon A. Diddy, formerly Medical Director and Superintendent of the Ahwahnee Sanatorium, Ahwahnee, California, has been appointed Director of Tuberculosis Control for Fresno County, California.

Dr. I. Zapolsky, formerly Medical Director and Superintendent, Mt. Vernon (Illinois) State Tuberculosis Sanatorium, has been appointed Superintendent and Medical Director of the State Tuberculosis Hospital, District Three, Paris, Kentucky.

ANNOUNCEMENTS

Due to the increase in printing and mailing costs the Editorial Board of the journal has been obliged to increase the annual price of the subscription rate of the College journal.

Effective with January 1953 and subsequent issues of DISEASES OF THE CHEST, the annual subscription rate will be $12.50. The price includes postage to any part of the world.

Grants for medical research totalling $264,424 have been appropriated for 1952 by the Lasdon Foundation. More than a score of institutions here and abroad will share in the grants.

The Foundation is a philanthropic organization established four years ago by the Lasdon brothers, William S., Milton S., Stanley S. and J. S., of New York, to support research exclusively in the fields of medicine and health.

Approximately 90 per cent of the grants were awarded to institutions for research in heart and lung disease.

1952 Directory Changes

Dr. Morrison H. Belmont of San Francisco, California, listed at 2495 Shattuck Avenue, Berkeley, California, should be corrected to read, 909 Hyde Street, San Francisco, California.

Dr. Henry A. Brodkin, Newark, New Jersey, was incorrectly designated as a diplomate of the American Board of Thoracic Surgery.

CORRECTION NOTICE

Dr. Hawley H. Seiler of Tampa, Florida, Program Chairman of the Florida Chapter for 1952-53, was named incorrectly in the September issue of the College journal.

Book Review

Diagnostic and Experimental Methods in Tuberculosis. By Henry Stuart Willis and Martin Marc Cummings. Charles C. Thomas, Springfield, Illinois. 2nd Edition. 1951.

The appearance of Diagnostic and Experimental Methods in Tuberculosis, by Henry Stuart Willis, in 1928, represented a landmark in the study of this disease. This edition has been almost completely rewritten as a result of the great advances, particularly in diagnostic methods and chemotherapy, that have emerged since the first edition was written. At that time tuberculosis was the foremost cause of death in this country, but was recognized usually in an advanced stage following the development of severe symptoms, and was treated mainly by rest and palliative measures. Now, chiefly as a result of the campaign against tuberculosis, to which this book and its authors have made such substantial contributions, tuberculosis is no longer numbered among the leading half-dozen causes of death in the United States, although it still kills millions every year in the entire world. It is now being detected at an early stage by mass screening methods, and active disease demonstrated by the cultivation of the bacilli by modern methods long before they could be found by the older microscopic techniques.

Experimental investigations into the treatment of tuberculosis was then mere random probing into the unknown, and the few workers in this field were often admonished to cease a hopeless quest, and to devote their energies to more profitable projects. Now chemotherapy founded on such researches has become an essential part of the treatment of most patients with tuberculosis, and millions of dollars are being expended on developing it by hardheaded business men and their host of highly trained and eager workers. The immunology of tuberculosis then appeared to be an academic exercise of idle contemplation, tuberculin a relic of an abandoned therapy, and of diagnostic value only in infancy, and vaccination another fad of a few Frenchmen. Now that more than forty million people all over the world have been tuberculin tested, and half of them vaccinated with BCG, in the most extensive organized medical program in history, it has become increasingly urgent that the production and administration of these agents, and the observation and interpretation of the results, be improved and standardized, and their phenomena better understood.

This volume not only contains detailed directions for the performance of scores of useful diagnostic tests and experimental procedures, and for the observation and recording of their results, but from a rich background of historic perspective and the extensive laboratory and clinical experiences of the authors presents an evaluation of their significance such as few others could afford. In the numerous disputed points in the laboratory study of tuberculosis, such as the life cycle of the bacillus, the significance of granules, the existence of filtrable forms, the range of dissociation, the taxonomy of non-pathogenic acid fast bacilli, the value of tuberculin and of vaccination, and the many technical details involved in the procedures described, the tyro will appreciate the authoritative guidance, while even dissenting experts will profit from the clear exposition of the authors views.

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†For additional evidence, turn to page 8.

. . . about its ability to concentrate in other tissues:

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. . . about its toxicity:

". . . the toxicity of the compound appears to be of the same order as that of procaine penicillin."[2]

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1. Barach, A.L., et al.: Advances in the Treatment of Non-Tuberculous Pulmonary Disease, Bull. New York Acad. Med. *28*:353 (June) 1952.
2. Flippin, H.F.: 'Neo-Penil', a Penicillin Ester with Unusual Pharmacologic and Clinical Properties, report distributed at the Chicago Session of the American Medical Association (June) 1952.
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4. Segal, M.S., et al.: The Therapy of Chronic Pulmonary Emphysema, GP, in press.

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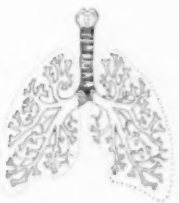

*T.M. Reg. U.S. Pat. Off. for penethamate hydriodide, S.K.F. (penicillin G diethylaminoethyl ester hydriodide)
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COLLEGE EVENTS

NATIONAL MEETINGS

Interim Session, American College of Chest Physicians, Denver, Colorado, November 30, December 1, 1952.

19th Annual Meeting, American College of Chest Physicians, Hotel New Yorker, New York City, May 28-31, 1953.

POSTGRADUATE MEETINGS

New York Postgraduate Course, November 10-15, 1952.

Utah Postgraduate Course, November 19-21, 1952.

Los Angeles Chest Disease Symposium, January 22-23, 1953.

Postgraduate Course, Diseases of the Chest for General Practitioners, Milwaukee, Wisconsin, March 4, 11, 18, 25, 1953.

Philadelphia Postgraduate Course, March 23-27, 1953.

CHAPTER MEETINGS

Southern Chapter Meeting, Miami, Florida, November 9-10, 1952.

Potomac Chapter Meeting, White Sulphur Springs, West Virginia, April 10, 1953.

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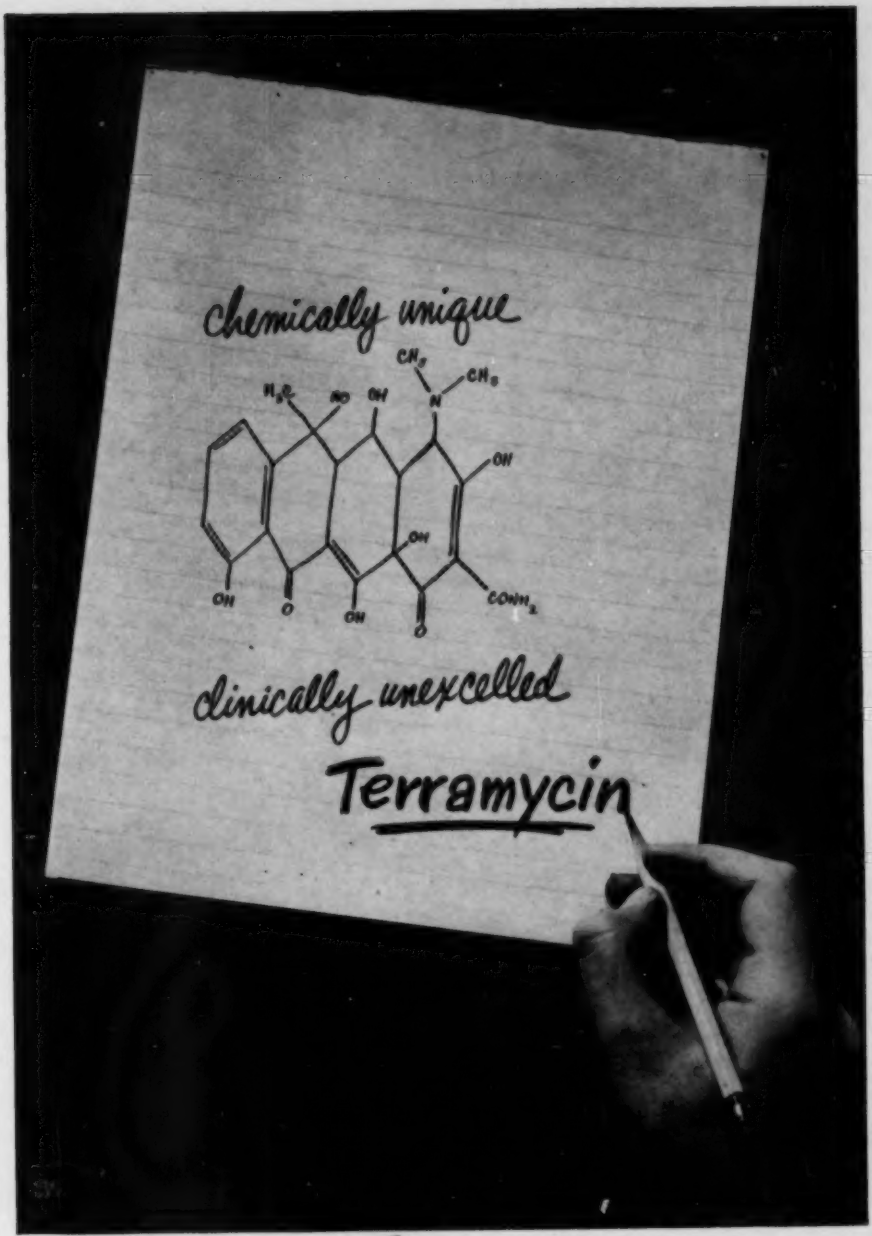

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